

OM protein - protein search, using sw model

Run on: July 26, 2004, 12:38:32 ; Search time 49.3333 Seconds  
(without alignments)  
3991.938 Million cell updates/sec

Title: US-09-806-194A-16  
Perfect score: 3651  
Sequence: 1 MLPGLALLLLAAWTARALEV.....QQNGYENPTYKFFEQMQNKK 697

Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5

Searched: 1586107 seqs, 282547505 residues

Total number of hits satisfying chosen parameters: 1586107

Minimum DB seq length: 0  
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

Database : A\_Geneseq\_29Jan04:\*  
1: geneseqp1980s:\*  
2: geneseqp1990s:\*  
3: geneseqp2000s:\*  
4: geneseqp2001s:\*  
5: geneseqp2002s:\*  
6: geneseqp2003as:\*  
7: geneseqp2003bs:\*  
8: geneseqp2004s:\*

Pred. No. is the number of results predicted by chance to have a  
score greater than or equal to the score of the result being printed,  
and is derived by analysis of the total score distribution.

#### SUMMARIES

Result No.	Score	%		DB	ID	Description
		Query	Match Length			
1	3651	100.0	697	3	AAy88428	Aay88428 Human APP
2	3651	100.0	697	4	AAU07208	Aau07208 Human bet
3	3651	100.0	697	4	AAE10635	Aae10635 Human amy
4	3651	100.0	697	4	AAE06865	Aae06865 Human amy
5	3651	100.0	697	4	AAE02587	Aae02587 Human amy
6	3651	100.0	697	4	AAU06609	Aau06609 Human Amy
7	3651	100.0	697	5	ABB78596	Abb78596 Human APP
8	3646	99.9	697	3	AAy88430	Aay88430 Human APP
9	3646	99.9	697	4	AAU07210	Aau07210 Human bet

10	3646	99.9	697	4	AAE10637	Aae10637	Human	amy
11	3646	99.9	697	4	AAE06867	Aae06867	Human	amy
12	3646	99.9	697	4	AAE02589	Aae02589	Human	amy
13	3646	99.9	697	4	AAU06611	Aau06611	Human	Amy
14	3646	99.9	697	5	ABB78598	Abb78598	Human	APP
15	3646	99.9	740	7	ADB87314	Adb87314	Human	amy
16	3646	99.9	740	7	ADB87312	Adb87312	Human	amy
17	3643	99.8	697	3	AAAY88429	Aay88429	Human	APP
18	3643	99.8	697	4	AAU07209	Aau07209	Human	bet
19	3643	99.8	697	4	AAE10636	Aae10636	Human	amy
20	3643	99.8	697	4	AAE06866	Aae06866	Human	amy
21	3643	99.8	697	4	AAE02588	Aae02588	Human	amy
22	3643	99.8	697	4	AAU06610	Aau06610	Human	Amy
23	3643	99.8	697	5	ABB78597	Abb78597	Human	APP
24	3641	99.7	695	1	AAP81692	Aap81692	Sequence	
25	3641	99.7	695	2	AAR26338	Aar26338	APP695.	3
26	3641	99.7	695	2	AAAY20233	Aay20233	Human	bet
27	3641	99.7	695	2	AAAY07221	Aay07221	Amyloid	p
28	3641	99.7	695	3	AAAY88434	Aay88434	Human	APP
29	3641	99.7	695	3	AAAY44705	Aay44705	Human	bet
30	3641	99.7	695	4	AAE10632	Aae10632	Human	wil
31	3641	99.7	695	4	AAE06862	Aae06862	Human	wil
32	3641	99.7	695	4	AAE02584	Aae02584	Human	amy
33	3641	99.7	695	4	AAU06606	Aau06606	Human	Amy
34	3641	99.7	695	5	ABB78593	Abb78593	Human	APP
35	3641	99.7	695	5	AAG68315	Aag68315	Human	amy
36	3641	99.7	695	5	ABG32721	Abg32721	Human	amy
37	3641	99.7	695	6	ABP97918	Abp97918	Amino	aci
38	3641	99.7	695	6	ABB99604	Abb99604	Amino	aci
39	3641	99.7	695	7	ADB87311	Adb87311	Human	amy
40	3641	99.7	695	7	ADB33519	Adb33519	Human	APP
41	3641	99.7	695	7	ADC65997	Adc65997	Human	APP
42	3638	99.6	695	2	AAAY49690	Aay49690	Human	bet
43	3636	99.6	695	2	AAW19481	Aaw19481	APP695	mu
44	3636	99.6	695	2	AAW19484	Aaw19484	APP695	mu
45	3636	99.6	695	2	AAW19498	Aaw19498	APP695	mu

# ALIGNMENTS

## RESULT 1

AAAY88428

ID AAY88428 standard; protein; 697 AA.

XX

AC AAY88428;

XX

DT 03-AUG-2000 (first entry)

XX

DE Human APP696-KK amino acid sequence.

XX

KW Aspartyl protease; aspartase; amyloid precursor protein; APP; Asp 2;

KW Alzheimer's disease; beta secretase site; APP696-KK.

XX

OS Homo sapiens.

XX

PN WO200017369-A2.

XX  
 PD 30-MAR-2000.  
 XX  
 PF 23-SEP-1999; 99WO-US020881.  
 XX  
 PR 24-SEP-1998; 98US-0101594P.  
 XX  
 PA (PHAA ) PHARMACIA & UPJOHN CO.  
 XX  
 PI Gurney ME, Bienkowski MJ, Heinrikson RL, Parodi LA, Yan R;  
 XX  
 DR WPI; 2000-303209/26.  
 DR N-PSDB; AAA15665.  
 XX  
 PT New enzyme designated human aspartase useful in research into Alzheimer's  
 PT Disease is capable of cleaving amyloid protein precursor at the beta  
 PT secretase site to produce amyloid beta peptide.  
 XX  
 PS Claim 132; Page 137-141; 183pp; English.  
 XX  
 CC This sequence represents a modified version of the human amyloid  
 CC precursor protein (APP) amino acid sequence. The sequence is used in an  
 CC example of the method of the invention, to show that modification of APP  
 CC increases beta amyloid protein processing. The invention relates to a  
 CC protease (e.g. Asp2) capable of cleaving the beta secretase site of  
 CC amyloid precursor protein (APP). The protease contains a sequence  
 CC encoding the amino acid sequence DTG and a sequence encoding DSG or DTG  
 CC separated by 100-300 amino acids. When mutated the APP gene causes an  
 CC autosomal dominant form of Alzheimer's disease. APP localises to the cell  
 CC surface membrane and have a single C-terminal transmembrane domain.  
 CC Proteolytic processing of APP produces the amyloid beta protein, which is  
 CC possibly very important in Alzheimer's disease. The invention includes a  
 CC nucleotide sequence encoding the protease, a vector containing the  
 CC nucleotide sequence, and a cell line comprising the vector. Methods for  
 CC screening for inhibitors of beta secretase activity are also given in the  
 CC invention. The human aspartase protein and nucleotide sequences and the  
 CC methods for identifying inhibitors of the protease, are useful in the  
 CC treatment of and research in to Alzheimer's disease  
 XX  
 SQ Sequence 697 AA;

Query Match 100.0%; Score 3651; DB 3; Length 697;  
 Best Local Similarity 100.0%; Pred. No. 1.4e-253;  
 Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPQLQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPQLQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180

Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDDEDGDEVEEEAEEPVEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDEDGDEVEEEAEEPVEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLVFVFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV	660
Db	601	RHDSGYEVHHQKLVFVFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697

RESULT 2

AAU07208

ID AAU07208 standard; protein; 697 AA.

XX

AC AAU07208;

XX

DT 24-OCT-2001 (first entry)

XX

DE Human beta-amyloid protein precursor, APP695-KK.

XX

KW Human; aspartyl protease 1; Asp-1; nootropic; neuroprotective;

KW aspartyl protease 2; Asp2; amyloid protein precursor; APP;

KW beta-secretase; Alzheimer's disease; APP695-KK.

XX

OS Homo sapiens.

XX

PN WO200149097-A2.

XX

PD 12-JUL-2001.

XX





Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAANERQQVLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAANERQQVLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK	697

# RESULT 3

AAE10635

ID AAE10635 standard; protein; 697 AA.

XX

AC AAE10635;

XX

DT 10-DEC-2001 (first entry)

XX

DE Human amyloid protein precursor 695-KK (APP695-KK) isoform.

XX

KW Human; aspartyl protease 1; Aspl; amyloid precursor protein; APP695-KK;

KW Alzheimer's disease; AD; dementia; neurofibrillary tangle; gliosis;

KW amyloid plaque; neuronal loss; proteolytic; nootropic; neuroprotective.

XX

OS Homo sapiens.

OS Synthetic.  
 XX  
 PN GB2357767-A.  
 XX  
 PD 04-JUL-2001.  
 XX  
 PF 22-SEP-2000; 2000GB-00023315.  
 XX  
 PR 23-SEP-1999; 99US-00404133.  
 PR 23-SEP-1999; 99US-0155493P.  
 PR 23-SEP-1999; 99WO-US020881.  
 PR 13-OCT-1999; 99US-00416901.  
 PR 06-DEC-1999; 99US-0169232P.  
 XX  
 PA (PHAA ) PHARMACIA & UPJOHN CO.  
 XX  
 PI Bienkowski MJ, Gurney M;  
 XX  
 DR WPI; 2001-444208/48.  
 DR N-PSDB; AAD17871.  
 XX  
 PT Polypeptide comprising fragments of human aspartyl protease with amyloid  
 PT precursor protein processing activity and alpha-secretase activity, for  
 PT identifying modulators useful in treating Alzheimer's disease.  
 XX  
 PS Example 6; Page 114-116; 187pp; English.  
 XX  
 CC The patent discloses human aspartyl protease 1 (hu-Asp1) or modified Asp1  
 CC proteins which lack transmembrane domain or amino terminal domain or  
 CC cytoplasmic domain and retains alpha-secretase activity and amyloid  
 CC protein precursor (APP) processing activity. The proteins of the  
 CC invention are useful for assaying hu-Asp1 alpha-secretase activity, which  
 CC in turn is useful for identifying modulators of hu-Asp1 alpha-secretase  
 CC activity, where modulators that increase hu-Asp1 alpha-secretase activity  
 CC are useful for treating Alzheimer's disease (AD) which causes progressive  
 CC dementia with consequent formation of amyloid plaques, neurofibrillary  
 CC tangles, gliosis and neuronal loss. Hu-Asp1 protease substrate is useful  
 CC for assaying hu-Asp1 proteolytic activity, by contacting hu-Asp1 protein  
 CC with the substrate under acidic conditions and determining the level of  
 CC hu-Asp1 proteolytic activity. The present sequence is human amyloid  
 CC protein precursor 695-KK (APP695-KK) isoform which is obtained by the  
 CC addition of two Lys residues (KK motif) at the C-terminus of APP695  
 CC protein  
 XX  
 SQ Sequence 697 AA;

Query Match 100.0%; Score 3651; DB 4; Length 697;  
 Best Local Similarity 100.0%; Pred. No. 1.4e-253;  
 Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```

Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
          |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
          |||
Db     61 TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

```

Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHREMSQVMREWEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHREMSQVMREWEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697

#### RESULT 4

AAE06865

ID AAE06865 standard; protein; 697 AA.

XX

AC AAE06865;

XX

DT 23-OCT-2001 (first entry)

XX

DE Human amyloid precursor protein 695-KK (APP695-KK) isoform.

XX

KW Human; aspartyl protease; Asp; beta-amyloid precursor protein 695-KK;

KW beta-secretase; Alzheimer's disease; dementia; amyloid plaque; gliosis;

KW neurofibrillary tangle; neuronal loss; amyloid-beta peptide; nootropic;

KW neuroprotective; antisense therapy; gene therapy; APP695-KK; mutant;

KW mutein.

```

XX OS Homo sapiens.
XX
XX PN WO200150829-A2.
XX
XX PD 19-JUL-2001.
XX
XX PF 09-MAY-2001; 2001WO-IB000799.
XX
XX PR 09-MAY-2001; 2001WO-IB000799.
XX
XX PA (BIEN/) BIENKOWSKI M J.
XX PA (GURN/) GURNEY M E.
XX PA (HEIN/) HEINRIKSON R L.
XX PA (PARO/) PARODI L A.
XX PA (YANR/) YAN R.
XX
XX PI Bienkowski MJ, Gurney ME, Heinrikson RL, Parodi LA, Yan R;
XX
XX DR WPI; 2001-483072/52.
XX DR N-PSDB; AAD13027.
XX
XX PT Novel purified polypeptide comprising fragment of mammalian aspartyl
XX PT protease 2, lacking Asp2 transmembrane domain and retaining beta
XX PT secretase activity of Asp2 useful for identifying inhibitors of Asp2
XX PT activity.
XX
XX PS Example 6; Page 144-146; 185pp; English.
XX
XX CC The invention relates to human aspartyl proteases (Hu-Asp), beta-amyloid
XX CC precursor protein (APP) isoforms and their corresponding DNA molecules.
XX CC Human aspartyl proteases can act as beta-secretase proteases useful for
XX CC treating Alzheimer's disease. APP isoforms are useful for identifying
XX CC modulators of amyloid-beta peptide production, for use in designing
XX CC therapeutics for the treatment and prevention of Alzheimer's disease,
XX CC dementia, formation of amyloid plaques, neurofibrillary tangles, gliosis
XX CC and neuronal loss. APP isoforms are also used in methods for identifying
XX CC inhibitors and modulators of human Asp2 activity. The invention relates
XX CC to a method for identifying agents that modulate the activity of human
XX CC aspartyl protease Asp2. Amyloid-beta peptides obtained from APP are used
XX CC as a means to screen in cellular assays for the inhibitors of beta- and
XX CC gamma- secretase. Hu-Asp DNA fragments are useful as probes or primers in
XX CC polymerase chain reactions (PCR). The probes are useful for detecting Hu-
XX CC Asp nucleic acids in in vitro assays and in Northern and Southern blots.
XX CC The present sequence is modified human amyloid precursor protein 695-KK
XX CC (APP695-KK) isoform. APP695-KK isoform is obtained by addition of two Lys
XX CC residues (KK motif) at the C-terminal end of APP695 isoform
XX
XX SQ Sequence 697 AA;

Query Match 100.0%; Score 3651; DB 4; Length 697;
Best Local Similarity 100.0%; Pred. No. 1.4e-253;
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLLNMHMNVQNGKWDSDPSGTK 60
Db 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLLNMHMNVQNGKWDSDPSGTK 60

```

Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDDGDEVEEEAEPEYEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDGDEVEEEAEPEYEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697

RESULT 5

AAE02587

ID AAE02587 standard; protein; 697 AA.

XX

AC AAE02587;

XX

DT 10-AUG-2001 (first entry)

XX

DE Human amyloid precursor protein 695-KK (APP695-KK).

XX

KW Human; alpha-secretase; amyloid precursor protein 695-KK; APP695-KK;

KW therapy; Alzheimer's disease; antialzheimer's.  
 XX  
 OS Homo sapiens.  
 OS Synthetic.  
 XX  
 PN WO200123533-A2.  
 XX  
 PD 05-APR-2001.  
 XX  
 PF 22-SEP-2000; 2000WO-US026080.  
 XX  
 PR 23-SEP-1999; 99US-0155493P.  
 PR 23-SEP-1999; 99WO-US020881.  
 PR 13-OCT-1999; 99US-00416901.  
 PR 06-DEC-1999; 99US-0169232P.  
 XX  
 PA (PHAA ) PHARMACIA & UPJOHN CO.  
 XX  
 PI Gurney M, Bienkowski MJ;  
 XX  
 DR WPI; 2001-290516/30.  
 DR N-PSDB; AAD06745.  
 XX  
 PT Enzymes that cleave the alpha-secretase site of the amyloid precursor  
 PT protein, useful for the treatment of Alzheimer's disease.  
 XX  
 PS Example 6; Page 143-145; 189pp; English.  
 XX  
 CC The present invention relates to enzymes for cleaving the alpha-  
 CC secretase site of the amyloid precursor protein (APP) and methods of  
 CC identifying those enzymes. The methods may be used to identify enzymes  
 CC that may be used to cleave the alpha-secretase cleavage site of the APP  
 CC protein. The enzymes may be used to treat or modulate the progress of  
 CC Alzheimer's disease. The present sequence is human APP695-KK. This  
 CC sequence contains two carboxy-terminal lysine residues  
 XX  
 SQ Sequence 697 AA;

Query Match 100.0%; Score 3651; DB 4; Length 697;  
 Best Local Similarity 100.0%; Pred. No. 1.4e-253;  
 Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240

Qy	241	EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFENMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFENMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLANMISEPRI SYGNDALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLANMISEPRI SYGNDALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV	660
Db	601	RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697

# RESULT 6

AAU06609

ID AAU06609 standard; protein; 697 AA.

XX

AC AAU06609;

XX

DT 24-OCT-2001 (first entry)

XX

DE Human Amyloid precursor protein mutant, APP695-KK.

XX

KW Human; Aspartyl protease; Asp2b; beta-secretase; nootropic;

KW neuroprotective; amyloid protein precursor; APP; Alzheimer's disease;

KW amyloid-beta; Abeta; APP695-KK; mutant; mutein.

XX

OS Homo sapiens.

XX

FH Key Location/Qualifiers

FT Misc-difference 696. .697

FT /note= "2 Extra Lys residues added compared to wild-type

FT APP695"

XX

PN WO200149098-A2.

XX



PD 12-JUL-2001.  
 XX  
 PF 09-MAY-2001; 2001WO-IB000798.  
 XX  
 PR 09-MAY-2001; 2001WO-IB000798.  
 XX  
 PA (BIEN/) BIENKOWSKI M J.  
 PA (GURN/) GURNEY M E.  
 PA (HEIN/) HEINRIKSON R L.  
 PA (PARO/) PARODI L A.  
 PA (YANR/) YAN R.  
 XX  
 PI Bienkowski MJ, Gurney ME, Heinrikson RL, Parodi LA, Yan R;  
 XX  
 DR WPI; 2001-502549/55.  
 DR N-PSDB; AAS11523.  
 XX  
 PT Novel purified polypeptide comprising fragment of mammalian aspartyl  
 PT protease 2, lacking Asp2 transmembrane domain and retaining beta  
 PT secretase activity of Asp2 useful for identifying inhibitors of Asp2  
 PT activity.  
 XX  
 PS Example 6; Page 144-146; 185pp; English.  
 XX  
 CC The invention relates to a purified polypeptide comprising a fragment of  
 CC mammalian aspartyl protease (Asp2) protein which lacks the Asp2  
 CC transmembrane domain and the Asp2 protein, and where the polypeptide and  
 CC the fragment retain the beta-secretase activity of the mammalian Asp2  
 CC protein. The invention also details polynucleotides for the Asp proteins  
 CC and vectors expressing them, and a polypeptide (isoform of amyloid  
 CC protein precursor (APP)) comprising the amino acid sequence of an APP or  
 CC its fragment containing an APP cleavage site recognizable by a mammalian  
 CC beta-secretase, and further comprising two lysine residues at the  
 CC carboxyl terminus of the amino acid sequence of the mammalian APP or APP  
 CC fragment. Also included in the invention are methods of identifying  
 CC modulators or inhibitors of Asp2. Modulators and inhibitors of Asp2 are  
 CC useful for treating Alzheimer's disease. APP is useful in methods for  
 CC identifying inhibitors or modulators of human Asp2 activity and amyloid-  
 CC beta (Abeta) peptide production. APP is also useful in designing  
 CC therapeutics for the treatment or prevention of Alzheimer's disease. APP  
 CC comprising the APP-Sw-beta-secretase peptide sequence (NLDA), which is  
 CC associated with increased levels of Abeta processing is useful in assays  
 CC relating the Alzheimer's research. The expression vector is useful for  
 CC recombinantly expressing APP. Nucleic acids that hybridise to Asp  
 CC oligonucleotides are useful as probes or primers. The probes are useful  
 CC for detecting Hu-Asp nucleic acids in in vitro assays and in Northern and  
 CC Southern blots. The present sequence is the human APP695 mutant, APP695-  
 CC KK which has 2 extra Lys residues added at the C-terminus compared to the  
 CC wild-type APP695. The mutation alters the specificity of the APP gamma-  
 CC secretase activity and increases the rate of processing of the amyloid  
 CC Abeta peptide  
 XX  
 SQ Sequence 697 AA;

Query Match 100.0%; Score 3651; DB 4; Length 697;  
 Best Local Similarity 100.0%; Pred. No. 1.4e-253;  
 Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVI PYRCLVG	120
Db	61	TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVI PYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDEDGDEVEEEAEEPYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDEDGDEVEEEAEEPYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697

RESULT 7

ABB78596

ID ABB78596 standard; protein; 697 AA.

XX

AC ABB78596;

XX

DT 16-JUL-2002 (first entry)

XX  
 DE Human APP695-KK protein sequence SEQ ID NO:16.  
 XX  
 KW Human; Asp-1; Asp-2; aspartyl protease; Alzheimer's disease; proteolytic;  
 KW amyloid precursor protein; APP.  
 XX  
 OS Homo sapiens.  
 XX  
 PN GB2367060-A.  
 XX  
 PD 27-MAR-2002.  
 XX  
 PF 29-OCT-2001; 2001GB-00025934.  
 XX  
 PR 23-SEP-1999; 99US-00404133.  
 PR 23-SEP-1999; 99US-0155493P.  
 PR 23-SEP-1999; 99WO-US020881.  
 PR 13-OCT-1999; 99US-00416901.  
 PR 06-DEC-1999; 99US-0169232P.  
 PR 22-SEP-2000; 2000GB-00023315.  
 XX  
 PA (PHAA ) PHARMACIA & UPJOHN CO.  
 XX  
 PI Bienkowski MJ, Gurney M;  
 XX  
 DR WPI; 2002-397167/43.  
 DR N-PSDB; ABL52463.  
 XX  
 PT Human aspartyl protease 1 substrates useful in assays to detect aspartyl  
 PT protease activity, e.g. for the diagnosis of Alzheimer's disease.  
 XX  
 PS Example 6; Page 114-116; 182pp; English.  
 XX  
 CC The present invention describes a human aspartyl protease 1 (hu-Asp1)  
 CC substrate (I) which comprises a peptide of no more than 50 amino acids,  
 CC and which comprises the 8 amino acid sequence Gly-Leu-Ala-Leu-Ala-Leu-  
 CC Glu-Pro. Also described are: (1) a method (II) for assaying hu-Asp1  
 CC proteolytic activity, comprising: (a) contacting a hu-Asp1 protein with  
 CC (I) under acidic conditions; and (b) determining the level of hu-Asp1  
 CC proteolytic activity; (2) a purified polynucleotide (III) comprising a  
 CC nucleotide sequence that hybridises under stringent conditions to the non  
 CC -coding strand complementary to a defined 1804 nucleotide sequence (see  
 CC ABL52456) where the nucleotide sequence encodes a polypeptide having Asp1  
 CC proteolytic activity and lacks nucleotides encoding a transmembrane  
 CC domain); (3) a purified polynucleotide (III') comprising a sequence that  
 CC hybridises under stringent conditions to (III) (the nucleotide sequence  
 CC encodes a polypeptide further lacking a pro-peptide domain corresponding  
 CC to amino acids 23-62 of hu-Asp1 (see ABB78589)); (4) a vector (IV)  
 CC comprising (III) or (III'); and (5) a host cell (V) transformed or  
 CC transfected with (III), (III') and/or (IV). The hu-Asp1 protease  
 CC substrate (I) may be used as an enzyme substrate in assays to detect  
 CC aspartyl protease activity, (II) and therefore diagnose diseases  
 CC associated with aberrant hu-Asp1 expression and activity such as  
 CC Alzheimer's disease. Hu-Asp1 has been localised to chromosome 21, while  
 CC hu-Asp2 has been localised to chromosome 11q23.3-24.1. The present  
 CC sequence represents human amyloid precursor protein APP695-KK, which is  
 CC given in an example from the present invention

XX

SQ Sequence 697 AA;

Query Match 100.0%; Score 3651; DB 5; Length 697;  
Best Local Similarity 100.0%; Pred. No. 1.4e-253;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
        |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
        |||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240
        |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240

Qy    241 EADDDDEDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
        |||
Db    241 EADDDDEDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360
        |||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVENMLK 420
        |||
Db    361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVENMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA 480
        |||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA 480

Qy    481 EEIQDEVDELLOKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL 540
        |||
Db    481 EEIQDEVDELLOKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600
        |||
Db    541 DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660
        |||
Db    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660

Qy    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697
        |||
Db    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697
```

RESULT 8

AA88430

ID AAY88430 standard; protein; 697 AA.

XX

AC AAY88430;

XX

DT 03-AUG-2000 (first entry)

XX

DE Human APP695-VF-KK amino acid sequence.

XX

KW Aspartyl protease; aspartase; amyloid precursor protein; APP; Asp 2;

KW Alzheimer's disease; beta secretase site; APP695-VF-KK.

XX

OS Homo sapiens.

XX

PN WO200017369-A2.

XX

PD 30-MAR-2000.

XX

PF 23-SEP-1999; 99WO-US020881.

XX

PR 24-SEP-1998; 98US-0101594P.

XX

PA (PHAA ) PHARMACIA & UPJOHN CO.

XX

PI Gurney ME, Bienkowski MJ, Heinrikson RL, Parodi LA, Yan R;

XX

DR WPI; 2000-303209/26.

DR N-PSDB; AAA15667.

XX

PT New enzyme designated human aspartase useful in research into Alzheimer's

PT Disease is capable of cleaving amyloid protein precursor at the beta

PT secretase site to produce amyloid beta peptide.

XX

PS Claim 133; Page 148-153; 183pp; English.

XX

CC This sequence represents a modified version of the human amyloid  
CC precursor protein (APP) amino acid sequence. The sequence is used in an  
CC example of the method of the invention, to show that modification of APP  
CC increases beta amyloid protein processing. The invention relates to a  
CC protease (e.g. Asp2) capable of cleaving the beta secretase site of  
CC amyloid precursor protein (APP). The protease contains a sequence  
CC encoding the amino acid sequence DTG and a sequence encoding DSG or DTG  
CC separated by 100-300 amino acids. When mutated the APP gene causes an  
CC autosomal dominant form of Alzheimer's disease. APP localises to the cell  
CC surface membrane and have a single C-terminal transmembrane domain.  
CC Proteolytic processing of APP produces the amyloid beta protein, which is  
CC possibly very important in Alzheimer's disease. The invention includes a  
CC nucleotide sequence encoding the protease, a vector containing the  
CC nucleotide sequence, and a cell line comprising the vector. Methods for  
CC screening for inhibitors of beta secretase activity are also given in the  
CC invention. The human aspartase protein and nucleotide sequences and the  
CC methods for identifying inhibitors of the protease, are useful in the  
CC treatment of and research in to Alzheimer's disease

XX

SQ Sequence 697 AA;

Query Match

99.9%; Score 3646; DB 3; Length 697;

Best Local Similarity 99.9%; Pred. No. 3.3e-253;  
Matches 696; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

```
Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGK 60
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EfvSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    121 EfvSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    181 GVEFVCCPLAEESDNVDSADAEEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDEDGDEVEEEAEPPYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    241 EADDDDEDEDGDEVEEEAEPPYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAEERQAKNLPKADKKAVIQHF 360
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAEERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy    481 EEIQDEVDPELLQKEQNYSDDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL 540
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    481 EEIQDEVDPELLQKEQNYSDDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    541 DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy    601 RHDSGYEVVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVLMLKKKQYTSIHHGV 660
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    601 RHDSGYEVVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVLMLKKKQYTSIHHGV 660

Qy    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697
        ||||||||||||||||||||||||||||||||||||||||
Db    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697
```

RESULT 9

AAU07210

ID AAU07210 standard; protein; 697 AA.

XX

AC AAU07210;

XX  
 DT 24-OCT-2001 (first entry)  
 XX  
 DE Human beta-amyloid protein precursor, APP695-VF-KK.  
 XX  
 KW Human; aspartyl protease 1; Asp-1; nootropic; neuroprotective;  
 KW aspartyl protease 2; Asp2; amyloid protein precursor; APP;  
 KW beta-secretase; Alzheimer's disease; APP695-VF-KK.  
 XX  
 OS Homo sapiens.  
 XX  
 FH Key Location/Qualifiers  
 FT Misc-difference 642  
 FT /note= "Wild type Val substituted by Phe"  
 XX  
 PN WO200149097-A2.  
 XX  
 PD 12-JUL-2001.  
 XX  
 PF 09-MAY-2001; 2001WO-IB000797.  
 XX  
 PR 09-MAY-2001; 2001WO-IB000797.  
 XX  
 PA (BIEN/) BIENKOWSKI M J.  
 PA (GURN/) GURNEY M E.  
 PA (HEIN/) HEINRIKSON R L.  
 PA (PARO/) PARODI L A.  
 PA (YANR/) YAN R.  
 XX  
 PI Bienkowski MJ, Gurney ME, Heinrikson RL, Parodi LA, Yan R;  
 XX  
 DR WPI; 2001-502548/55.  
 DR N-PSDB; AAS11710.  
 XX  
 PT Novel purified polypeptide comprising fragment of mammalian aspartyl  
 PT protease 2, lacking Asp2 transmembrane domain and retaining beta  
 PT secretase activity of Asp2 useful for identifying inhibitors of Asp2  
 PT activity.  
 XX  
 PS Example 8; Page 150-152; 185pp; English.  
 XX  
 CC The invention relates to a novel purified polypeptide comprising a  
 CC fragment of mammalian aspartyl protease 2 (Asp2) protein which lacks the  
 CC Asp2 transmembrane domain and the Asp2 protein, and where the polypeptide  
 CC and the fragment retain the beta-secretase activity of the mammalian Asp2  
 CC protein. Also included is an isoform of amyloid protein precursor (APP)  
 CC comprising the amino acid sequence of a APP or its fragment containing an  
 CC APP cleavage site recognisable by a mammalian beta-secretase, and further  
 CC comprising two lysine residues at the carboxyl terminus of the amino acid  
 CC sequence of the mammalian APP or APP fragment. The polypeptides are used  
 CC for assaying for modulators of beta-secretase activity; identifying  
 CC agents that inhibit the APP processing activity of human Asp2 aspartyl  
 CC protease (Hu-Asp2); identifying agents that modulate the activity of Asp2  
 CC ; and for reducing cellular production of amyloid beta (Abeta) from APP.  
 CC Agents identified by the above methods are useful for treating  
 CC Alzheimer's disease; and for identifying modulators of amyloid-beta  
 CC (Abeta) peptide production, for use in designing therapeutics for the

CC treatment or prevention of Alzheimer's disease. Probes and primers  
CC derived from Asp nucleic acid sequences are useful for detecting Hu-Asp  
CC nucleic acids in in vitro assays and in Northern and Southern blots. The  
CC present sequence represents the amino acid sequence of human amyloid  
CC protein precursor, APP695-VF-KK, used in the method of the invention

XX

SQ Sequence 697 AA;

Query Match 99.9%; Score 3646; DB 4; Length 697;  
Best Local Similarity 99.9%; Pred. No. 3.3e-253;  
Matches 696; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

```
Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPQLITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     61 TCIDTKEGILQYCQEVYPQLITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDEDGDEVEEEAEPEYEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    241 EADDDDEDEDGDEVEEEAEPEYEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPPAVA 480
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPPAVA 480

Qy    481 EEIQDEVDPELLQKEQNYSDDLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    481 EEIQDEVDPELLQKEQNYSDDLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHHGV 660

Qy    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697
```





CC activity, where modulators that increase hu-Asp1 alpha-secretase activity  
 CC are useful for treating Alzheimer's disease (AD) which causes progressive  
 CC dementia with consequent formation of amyloid plaques, neurofibrillary  
 CC tangles, gliosis and neuronal loss. Hu-Asp1 protease substrate is useful  
 CC for assaying hu-Asp1 proteolytic activity, by contacting hu-Asp1 protein  
 CC with the substrate under acidic conditions and determining the level of  
 CC hu-Asp1 proteolytic activity. The present sequence is human amyloid  
 CC protein precursor 695-VF-KK (APP695-VF-KK) isoform. This sequence is  
 CC obtained by the addition of two lysine residues (KK motif) at the C-  
 CC terminus of App695-VF isoform which is generated by the London mutation  
 CC in APP695, where Val at position 642 is replaced with Phe. APP695-VF-KK  
 CC isoform is useful for assaying the beta-secretase activity of human  
 CC aspartyl protease 2a (hu-Asp2a) protein

XX

SQ Sequence 697 AA;

Query Match 99.9%; Score 3646; DB 4; Length 697;  
 Best Local Similarity 99.9%; Pred. No. 3.3e-253;  
 Matches 696; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDEDGDEVEEEAEEPYEEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDEDGDEVEEEAEEPYEEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600

```

      |||
Db      541 DDLQPWHSFGADSVPA NTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600
Qy      601 RHDSGYEVHHQKL VFFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660
      |||
Db      601 RHDSGYEVHHQKL VFFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHHGV 660
Qy      661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697
      |||
Db      661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697

```

RESULT 11

AAE06867

ID AAE06867 standard; protein; 697 AA.

XX

AC AAE06867;

XX

DT 23-OCT-2001 (first entry)

XX

DE Human amyloid precursor protein 695-VF-KK (APP695-VF-KK) isoform.

XX

KW Human; aspartyl protease; Asp; beta-amyloid precursor protein 695-VF-KK;

KW beta-secretase; Alzheimer's disease; dementia; amyloid plaque; gliosis;

KW neurofibrillary tangle; neuronal loss; amyloid-beta peptide; nootropic;

KW neuroprotective; antisense therapy; gene therapy; APP695-VF-KK; mutant;

KW mutein.

XX

OS Homo sapiens.

OS Synthetic.

XX

FH Key Location/Qualifiers

FT Misc-difference 642

FT /note= "Wild type Val substituted with Phe"

XX

PN WO200150829-A2.

XX

PD 19-JUL-2001.

XX

PF 09-MAY-2001; 2001WO-IB000799.

XX

PR 09-MAY-2001; 2001WO-IB000799.

XX

PA (BIEN/) BIENKOWSKI M J.

PA (GURN/) GURNEY M E.

PA (HEIN/) HEINRIKSON R L.

PA (PARO/) PARODI L A.

PA (YANR/) YAN R.

XX

PI Bienkowski MJ, Gurney ME, Heinrikson RL, Parodi LA, Yan R;

XX

DR WPI; 2001-483072/52.

DR N-PSDB; AAD13029.

XX

PT Novel purified polypeptide comprising fragment of mammalian aspartyl

PT protease 2, lacking Asp2 transmembrane domain and retaining beta

PT secretase activity of Asp2 useful for identifying inhibitors of Asp2

PT activity.

XX

PS Example 8; Page 150-152; 185pp; English.

XX

CC The invention relates to human aspartyl proteases (Hu-Asp), beta-amyloid  
CC precursor protein (APP) isoforms and their corresponding DNA molecules.  
CC Human aspartyl proteases can act as beta-secretase proteases useful for  
CC treating Alzheimer's disease. APP isoforms are useful for identifying  
CC modulators of amyloid-beta peptide production, for use in designing  
CC therapeutics for the treatment and prevention of Alzheimer's disease,  
CC dementia, formation of amyloid plaques, neurofibrillary tangles, gliosis  
CC and neuronal loss. APP isoforms are also used in methods for identifying  
CC inhibitors and modulators of human Asp2 activity. The invention relates  
CC to a method for identifying agents that modulate the activity of human  
CC aspartyl protease Asp2. Amyloid-beta peptides obtained from APP are used  
CC as a means to screen in cellular assays for the inhibitors of beta- and  
CC gamma- secretase. Hu-Asp DNA fragments are useful as probes or primers in  
CC polymerase chain reactions (PCR). The probes are useful for detecting Hu-  
CC Asp nucleic acids in in vitro assays and in Northern and Southern blots.  
CC The present sequence is modified human amyloid precursor protein 695-VF-  
CC KK (APP695-VF-KK) isoform. APP695-VF-KK isoform is obtained by addition  
CC of two Lys residues (KK motif) at the C-terminal end of APP695-VF  
CC isoform. APP695-VF isoform is obtained by London V-F mutation in APP695  
CC isoform, where Val at position 642 is replaced with Phe. APP695-VF-KK  
CC isoform is useful for assaying the beta-secretase activity of human  
CC aspartyl protease 2a (Hu-Asp2a) protein

XX

SQ Sequence 697 AA;

Query Match 99.9%; Score 3646; DB 4; Length 697;  
Best Local Similarity 99.9%; Pred. No. 3.3e-253;  
Matches 696; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLLNMHMNVQNGKWSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLLNMHMNVQNGKWSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Qy	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360

Qy 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420  
 |||  
 Db 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480  
 |||  
 Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy 481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL 540  
 |||  
 Db 481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL 540

Qy 541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600  
 |||  
 Db 541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV 660  
 |||  
 Db 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHGGV 660

Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697  
 |||  
 Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697

RESULT 12

AAE02589

ID AAE02589 standard; protein; 697 AA.

XX

AC AAE02589;

XX

DT 10-AUG-2001 (first entry)

XX

DE Human amyloid precursor protein 695-VF-KK (APP695-VF-KK).

XX

KW Human; alpha-secretase; therapy; amyloid precursor protein 695-VF-KK;

KW APP695-VF-KK; Alzheimer's disease; antialzheimer's.

XX

OS Homo sapiens.

OS Synthetic.

XX

PN WO200123533-A2.

XX

PD 05-APR-2001.

XX

PF 22-SEP-2000; 2000WO-US026080.

XX

PR 23-SEP-1999; 99US-0155493P.

PR 23-SEP-1999; 99WO-US020881.

PR 13-OCT-1999; 99US-00416901.

PR 06-DEC-1999; 99US-0169232P.

XX

PA (PHAA ) PHARMACIA & UPJOHN CO.

XX

PI Gurney M, Bienkowski MJ;

XX

DR WPI; 2001-290516/30.

XX

XX

XX

XX

Qy

Db

Ov

Db

QY

Db

Qy

Db

Qy

Db

Qy

Db

Qy

Db

Qy

Db

Ov

Db

481 EEIODEVDELLOKEONYSDDVLANMISEPRI SYGNDALMPSLTETKTTVELLPVNGEFSL 540

Qy 541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600  
 |||  
 Db 541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV 660  
 |||  
 Db 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHGGV 660

Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697  
 |||  
 Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697

RESULT 13

AAU06611

ID AAU06611 standard; protein; 697 AA.

XX

AC AAU06611;

XX

DT 24-OCT-2001 (first entry)

XX

DE Human Amyloid precursor protein mutant, APP695-VF-KK.

XX

KW Human; Aspartyl protease; Asp2b; beta-secretase; nootropic;  
 KW neuroprotective; amyloid protein precursor; APP; Alzheimer's disease;  
 KW amyloid-beta; Abeta; APP695-VF-KK; London mutant; mutant; mutein.

XX

OS Homo sapiens.

XX

FH Key Location/Qualifiers

FT Misc-difference 642

FT /note= "Wild-type Val substituted by Phe"

FT Misc-difference 696. .697

FT /note= "2 Extra Lys residues added compared to wild-type

FT APP695"

XX

PN WO200149098-A2.

XX

PD 12-JUL-2001.

XX

PF 09-MAY-2001; 2001WO-IB000798.

XX

PR 09-MAY-2001; 2001WO-IB000798.

XX

PA (BIEN/) BIENKOWSKI M J.

PA (GURN/) GURNEY M E.

PA (HEIN/) HEINRIKSON R L.

PA (PARO/) PARODI L A.

PA (YANR/) YAN R.

XX

PI Bienkowski MJ, Gurney ME, Heinrikson RL, Parodi LA, Yan R;

XX

DR WPI; 2001-502549/55.

DR N-PSDB; AAS11525.

XX

PT Novel purified polypeptide comprising fragment of mammalian aspartyl





Db	241	EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMMLKKKQYTSIHGGV	660
Db	601	RHDSGYEVHHQKLFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMMLKKKQYTSIHGGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK	697

RESULT 14

ABB78598

ID ABB78598 standard; protein; 697 AA.

XX

AC ABB78598;

XX

DT 16-JUL-2002 (first entry)

XX

DE Human APP695-VF-KK protein sequence SEQ ID NO:20.

XX

KW Human; Asp-1; Asp-2; aspartyl protease; Alzheimer's disease; proteolytic; amyloid precursor protein; APP.

XX

OS Homo sapiens.

XX

PN GB2367060-A.

XX

PD 27-MAR-2002.

XX

PF 29-OCT-2001; 2001GB-00025934.

XX

PR 23-SEP-1999; 99US-00404133.

PR 23-SEP-1999; 99US-0155493P.

PR 23-SEP-1999; 99WO-US020881.

PR 13-OCT-1999; 99US-00416901.

PR 06-DEC-1999; 99US-0169232P.  
PR 22-SEP-2000; 2000GB-00023315.  
XX  
PA (PHAA ) PHARMACIA & UPJOHN CO.  
XX  
PI Bienkowski MJ, Gurney M;  
XX  
DR WPI; 2002-397167/43.  
DR N-PSDB; ABL52465.  
XX  
PT Human aspartyl protease 1 substrates useful in assays to detect aspartyl  
PT protease activity, e.g. for the diagnosis of Alzheimer's disease.  
XX  
PS Example 8; Page 120-122; 182pp; English.  
XX  
CC The present invention describes a human aspartyl protease 1 (hu-Asp1)  
CC substrate (I) which comprises a peptide of no more than 50 amino acids,  
CC and which comprises the 8 amino acid sequence Gly-Leu-Ala-Leu-Ala-Leu-  
CC Glu-Pro. Also described are: (1) a method (II) for assaying hu-Asp1  
CC proteolytic activity, comprising: (a) contacting a hu-Asp1 protein with  
CC (I) under acidic conditions; and (b) determining the level of hu-Asp1  
CC proteolytic activity; (2) a purified polynucleotide (III) comprising a  
CC nucleotide sequence that hybridises under stringent conditions to the non  
CC -coding strand complementary to a defined 1804 nucleotide sequence (see  
CC ABL52456) where the nucleotide sequence encodes a polypeptide having Asp1  
CC proteolytic activity and lacks nucleotides encoding a transmembrane  
CC domain); (3) a purified polynucleotide (III') comprising a sequence that  
CC hybridises under stringent conditions to (III) (the nucleotide sequence  
CC encodes a polypeptide further lacking a pro-peptide domain corresponding  
CC to amino acids 23-62 of hu-Asp1 (see ABB78589)); (4) a vector (IV)  
CC comprising (III) or (III'); and (5) a host cell (V) transformed or  
CC transfected with (III), (III') and/or (IV). The hu-Asp1 protease  
CC substrate (I) may be used as an enzyme substrate in assays to detect  
CC aspartyl protease activity, (II) and therefore diagnose diseases  
CC associated with aberrant hu-Asp1 expression and activity such as  
CC Alzheimer's disease. Hu-Asp1 has been localised to chromosome 21, while  
CC hu-Asp2 has been localised to chromosome 11q23.3-24.1. The present  
CC sequence represents human amyloid precursor protein APP695-VF-KK, which  
CC is given in an example from the present invention  
XX  
SQ Sequence 697 AA;

Query Match 99.9%; Score 3646; DB 5; Length 697;  
Best Local Similarity 99.9%; Pred. No. 3.3e-253;  
Matches 696; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGK	60
Qy	61	TCIDTKEGILQYCQEVYPQLQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPQLQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180

Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Qy	241	EADDDDEDEDGDEVEEEAEEPYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDEDGDEVEEEAEEPYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRRLALENYITALQAVPPRRPHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRRLALENYITALQAVPPRRPHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGHV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGHV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK	697

RESULT 15

ADB87314

ID ADB87314 standard; protein; 740 AA.

XX

AC ADB87314;

XX

DT 04-DEC-2003 (first entry)

XX

DE Human amyloid A4 precursor (APP) Swedish mutant protein with tags.

XX

KW amyloid precursor protein; APP; amino acid tag; gamma-secretase;

KW alpha-secretase; beta-secretase; C-terminal cleavage product; gammaCTF;

KW presenilin 1; Alzheimer's disease; beta-amyloid; senile plaque;

KW secretase inhibitor; APP biosynthesis; APP activity; human;

KW amyloid A4 precursor; Swedish mutant; mutant; mutein.

XX

OS Homo sapiens.

XX

FH Key Location/Qualifiers

FT Misc-difference 595  
 FT /note= "Wild-type Lys substituted by Asn"  
 FT Misc-difference 596  
 FT /note= "Wild-type Met substituted by Leu"  
 FT Cleavage-site 645. .646  
 FT /note= "Cleavage of the APP protein between these two  
 FT residues by gamma-secretase produces gammaCTF"  
 FT Region 718. .731  
 FT /label= V5\_epitope\_tag  
 FT Region 735. .740  
 FT /label= Polyhistidine\_tag  
 XX  
 PN WO2003064681-A2.  
 XX  
 PD 07-AUG-2003.  
 XX  
 PF 31-JAN-2003; 2003WO-GB000433.  
 XX  
 PR 31-JAN-2002; 2002GB-00002276.  
 XX  
 PA (EISA ) EISAI LONDON RES LAB LTD.  
 XX  
 PI Lucas FR, Taylor J;  
 XX  
 DR WPI; 2003-663492/62.  
 XX  
 PT New protein comprising an amyloid precursor protein and an amino acid  
 PT tag, useful for screening or identifying therapeutic compounds,  
 PT particularly secretase inhibitors, useful for the treatment of diseases  
 PT e.g. Alzheimer's disease.  
 XX  
 PS Claim 4; Page; 24pp; English.  
 XX  
 CC This invention relates to a novel protein which comprises an amyloid  
 CC precursor protein (APP) and an amino acid tag. The present invention also  
 CC relates to assays for measuring gamma-secretase activity and/or  
 CC simultaneously measuring alpha, beta or gamma-secretase activity which  
 CC involve utilising the stabilisation of the gamma-secretase C-terminal  
 CC cleavage product of APP (gamma C-terminal fragment of APP; gammaCTF).  
 CC GammaCTF is generated by the action of gamma-secretase/presenilin 1, an  
 CC important enzyme in Alzheimer's disease. GammaCTF is the sister product  
 CC of beta-amyloid which is produced by the same process and accumulates in  
 CC senile plaques in Alzheimer's disease. The protein or the methods of the  
 CC invention may be useful for screening a test compound for its ability to  
 CC modulate alpha, beta or gamma-secretase activity. In particular, the  
 CC protein or methods are useful for screening or testing secretase  
 CC inhibitors, and differentiating such inhibitors from agents that act  
 CC indirectly, for example interface with normal APP biosynthesis and  
 CC activity. The amino acid tag of the new protein is useful for the  
 CC stabilisation of gamma-secretase cleavage products of APP. Specifically,  
 CC the protein or methods may be useful for screening or identifying  
 CC therapeutic compounds or compositions for the treatment of diseases such  
 CC as Alzheimer's disease. The present sequence is that of the Swedish  
 CC mutant human amyloid A4 precursor (APP) of the invention, tagged with a  
 CC V5 epitope tag and a polyhistidine tag, which was expressed in KEK293  
 CC cells during the exemplification of the invention. Note: This sequence  
 CC does not appear in the specification but was created by the indexer from

CC information given.  
XX  
SQ Sequence 740 AA;

Query Match 99.9%; Score 3646; DB 7; Length 740;  
Best Local Similarity 100.0%; Pred. No. 3.6e-253;  
Matches 696; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAANERQQVLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAANERQQVLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNK	696
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNK	696

Search completed: July 26, 2004, 12:43:58  
Job time : 52.3333 secs

GenCore version 5.1.6  
Copyright (c) 1993 - 2004 Compugen Ltd.

OM protein - protein search, using sw model

Run on: July 26, 2004, 12:41:23 ; Search time 15 Seconds  
(without alignments)  
2398.887 Million cell updates/sec

Title: US-09-806-194A-16  
Perfect score: 3651  
Sequence: 1 MLPGLALLLLAAWTARALEV.....QQNGYENPTYKFFEQMQNKK 697

Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5

Searched: 389414 seqs, 51625971 residues

Total number of hits satisfying chosen parameters: 389414

Minimum DB seq length: 0  
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

Database : Issued\_Patents\_AA:\*  
1: /cgn2\_6/ptodata/2/iaa/5A\_COMB.pep:\*  
2: /cgn2\_6/ptodata/2/iaa/5B\_COMB.pep:\*  
3: /cgn2\_6/ptodata/2/iaa/6A\_COMB.pep:\*  
4: /cgn2\_6/ptodata/2/iaa/6B\_COMB.pep:\*  
5: /cgn2\_6/ptodata/2/iaa/PCTUS\_COMB.pep:\*  
6: /cgn2\_6/ptodata/2/iaa/backfiles1.pep:\*

Pred. No. is the number of results predicted by chance to have a  
score greater than or equal to the score of the result being printed,  
and is derived by analysis of the total score distribution.

SUMMARIES

		%					Description
Result	Query	Match	Length	DB	ID		
No.	Score						
1	3651	100.0	697	4	US-09-548-372D-16	Sequence 16, Appl	
2	3651	100.0	697	4	US-09-548-367D-16	Sequence 16, Appl	
3	3651	100.0	697	4	US-09-551-853D-16	Sequence 16, Appl	
4	3646	99.9	697	4	US-09-548-372D-20	Sequence 20, Appl	
5	3646	99.9	697	4	US-09-548-367D-20	Sequence 20, Appl	
6	3646	99.9	697	4	US-09-551-853D-20	Sequence 20, Appl	
7	3643	99.8	697	4	US-09-548-372D-18	Sequence 18, Appl	
8	3643	99.8	697	4	US-09-548-367D-18	Sequence 18, Appl	
9	3643	99.8	697	4	US-09-551-853D-18	Sequence 18, Appl	
10	3641	99.7	695	1	US-08-123-702-2	Sequence 2, Appli	
11	3641	99.7	695	2	US-08-104-165-1	Sequence 1, Appli	

12	3641	99.7	695	3	US-08-464-250-1	Sequence 1, Appli
13	3641	99.7	695	4	US-08-464-250-1	Sequence 1, Appli
14	3641	99.7	695	4	US-09-458-481B-7	Sequence 7, Appli
15	3641	99.7	695	4	US-09-458-481B-8	Sequence 8, Appli
16	3641	99.7	695	4	US-09-548-372D-10	Sequence 10, Appl
17	3641	99.7	695	4	US-09-548-367D-10	Sequence 10, Appl
18	3641	99.7	695	4	US-09-551-853D-10	Sequence 10, Appl
19	3641	99.7	695	4	US-09-415-099-6	Sequence 6, Appli
20	3641	99.7	695	6	5218100-2	Patent No. 5218100
21	3636	99.6	695	4	US-09-548-372D-14	Sequence 14, Appl
22	3636	99.6	695	4	US-09-548-367D-14	Sequence 14, Appl
23	3636	99.6	695	4	US-09-551-853D-14	Sequence 14, Appl
24	3635	99.6	694	1	US-08-339-152A-18	Sequence 18, Appl
25	3635	99.6	694	2	US-08-007-999B-5	Sequence 5, Appli
26	3635	99.6	694	2	US-08-689-276A-5	Sequence 5, Appli
27	3633	99.5	695	4	US-09-548-372D-12	Sequence 12, Appl
28	3633	99.5	695	4	US-09-548-367D-12	Sequence 12, Appl
29	3633	99.5	695	4	US-09-551-853D-12	Sequence 12, Appl
30	3629	99.4	695	1	US-08-371-930-27	Sequence 27, Appl
31	3629	99.4	695	5	PCT-US94-01712-27	Sequence 27, Appl
32	3617	99.1	695	1	US-08-339-152A-30	Sequence 30, Appl
33	3612	98.9	753	4	US-09-548-372D-61	Sequence 61, Appl
34	3612	98.9	753	4	US-09-548-367D-61	Sequence 61, Appl
35	3612	98.9	753	4	US-09-551-853D-61	Sequence 61, Appl
36	3602	98.7	751	1	US-08-123-702-4	Sequence 4, Appli
37	3602	98.7	751	2	US-08-104-165-2	Sequence 2, Appli
38	3602	98.7	751	2	US-08-422-333-2	Sequence 2, Appli
39	3602	98.7	751	2	US-08-422-333-21	Sequence 21, Appl
40	3602	98.7	751	3	US-08-464-250-2	Sequence 2, Appli
41	3602	98.7	751	4	US-08-464-250-2	Sequence 2, Appli
42	3602	98.7	751	4	US-08-832-867-5	Sequence 5, Appli
43	3602	98.7	751	4	US-09-548-372D-57	Sequence 57, Appl
44	3602	98.7	751	4	US-09-548-367D-57	Sequence 57, Appl
45	3602	98.7	751	4	US-09-551-853D-57	Sequence 57, Appl

#### ALIGNMENTS

#### RESULT 1

US-09-548-372D-16

; Sequence 16, Application US/09548372D

; Patent No. 6420534

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR AND USES

; TITLE OF INVENTION: THEREOF

; FILE REFERENCE: 29915/6280I

; CURRENT APPLICATION NUMBER: US/09/548,372D

; CURRENT FILING DATE: 2000-04-12

; PRIOR APPLICATION NUMBER: US 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23



; PRIOR APPLICATION NUMBER: US 60/101,594  
; PRIOR FILING DATE: 1998-09-24  
; NUMBER OF SEQ ID NOS: 73  
; SOFTWARE: PatentIn version 3.1  
; SEQ ID NO 16  
; LENGTH: 697  
; TYPE: PRT  
; ORGANISM: Homo sapiens  
US-09-548-372D-16

Query Match 100.0%; Score 3651; DB 4; Length 697;  
Best Local Similarity 100.0%; Pred. No. 1.4e-266;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGHV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGHV	660

Qy 661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMQNKK 697  
 |||  
 Db 661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMQNKK 697

```

RESULT 2
US-09-548-367D-16
; Sequence 16, Application US/09548367D
; Patent No. 6440698
; GENERAL INFORMATION:
; APPLICANT: GURNEY ET AL.
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR
AND USES
; TITLE OF INVENTION:  THEREOF
; FILE REFERENCE: 29915/6280H
; CURRENT APPLICATION NUMBER: US/09/548,367D
; CURRENT FILING DATE: 2000-04-12
; PRIOR APPLICATION NUMBER: US 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 16
; LENGTH: 697
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-548-367D-16

```

Query Match 100.0%; Score 3651; DB 4; Length 697;  
Best Local Similarity 100.0%; Pred. No. 1.4e-266;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRILNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRILNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDDGDEVEEEAEPEYEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDGDEVEEEAEPEYEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300

Qy 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360  
 |||  
 Db 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360

Qy 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420  
 |||  
 Db 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA 480  
 |||  
 Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA 480

Qy 481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540  
 |||  
 Db 481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540

Qy 541 DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600  
 |||  
 Db 541 DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGHV 660  
 |||  
 Db 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGHV 660

Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697  
 |||  
 Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697

RESULT 3

US-09-551-853D-16

; Sequence 16, Application US/09551853D

; Patent No. 6500667

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR  
 AND USES

; TITLE OF INVENTION: THEREOF

; FILE REFERENCE: 29915/6280L

; CURRENT APPLICATION NUMBER: US/09/551,853D

; CURRENT FILING DATE: 2000-04-18

; PRIOR APPLICATION NUMBER: US 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn version 3.1

; SEQ ID NO 16

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-551-853D-16

Query Match 100.0%; Score 3651; DB 4; Length 697;  
Best Local Similarity 100.0%; Pred. No. 1.4e-266;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEEDSDVWGGADTDYADGSEDKVVEVAEEEEVAEEEE 240
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    181 GVEFVCCPLAEESDNVDSADAEEEDSDVWGGADTDYADGSEDKVVEVAEEEEVAEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEEPYEEATERTTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV 300
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    241 EADDDDEDDEDGDEVEEEAEEPYEEATERTTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAAENERQQLVETHMARVEAMLNDRRRLALENYITALQAVPPRPRHVFNMLK 420
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    361 QEKVESLEQEAAENERQQLVETHMARVEAMLNDRRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy    481 EEIQDEVDELLQKEQNYSDDLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL 540
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    481 EEIQDEVDELLQKEQNYSDDLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV 660
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV 660

Qy    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697
      ||||||||||||||||||||||||||||||||||||||||
Db    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697
```

RESULT 4  
US-09-548-372D-20  
; Sequence 20, Application US/09548372D



Qy 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480  
 |||  
 Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy 481 EEIQDEVDELLQKEQNYSDDLANMISEPRISYGNLMPSLTETKTTVELLPVNGEFSL 540  
 |||  
 Db 481 EEIQDEVDELLQKEQNYSDDLANMISEPRISYGNLMPSLTETKTTVELLPVNGEFSL 540

Qy 541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600  
 |||  
 Db 541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV 660  
 |||  
 Db 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV 660

Qy 661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMKNKK 697  
 |||  
 Db 661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMKNKK 697

RESULT 5

US-09-548-367D-20

; Sequence 20, Application US/09548367D

; Patent No. 6440698

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR AND USES

; TITLE OF INVENTION: THEREOF

; FILE REFERENCE: 29915/6280H

; CURRENT APPLICATION NUMBER: US/09/548,367D

; CURRENT FILING DATE: 2000-04-12

; PRIOR APPLICATION NUMBER: US 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn version 3.1

; SEQ ID NO 20

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-548-367D-20

Query Match 99.9%; Score 3646; DB 4; Length 697;

Best Local Similarity 99.9%; Pred. No. 3.4e-266;

Matches 696; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

Qy 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60  
 |||  
 Db 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLP CGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLP CGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDDEDGDEVEEEAE EEPYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDEDGDEVEEEAE EEPYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWE EAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWE EAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQE AANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVF NMLK	420
Db	361	QEKVESLEQE AANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVF NMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSL SLLYNPVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSL SLLYNPVA	480
Qy	481	EEIQDEVDEL LQKEQNYSDDLANMISEPRISYGNDALMP SLTETKT'TVELLPVNGE FSL	540
Db	481	EEIQDEVDEL LQKEQNYSDDLANMISEPRISYGNDALMP SLTETKT'TVELLPVNGE FSL	540
Qy	541	DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEE ISEVKMDAEF	600
Db	541	DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEE ISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Db	601	RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697

RESULT 6

US-09-551-853D-20

; Sequence 20, Application US/09551853D

; Patent No. 6500667

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR AND USES

; TITLE OF INVENTION: THEREOF

; FILE REFERENCE: 29915/6280L

; CURRENT APPLICATION NUMBER: US/09/551,853D

; CURRENT FILING DATE: 2000-04-18

```
; PRIOR APPLICATION NUMBER: US 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 20
; LENGTH: 697
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-551-853D-20
```

```
Query Match          99.9%; Score 3646; DB 4; Length 697;
Best Local Similarity 99.9%; Pred. No. 3.4e-266;
Matches 696; Conservative 0; Mismatches 1; Indels 0; Gaps 0;
```

```
Qy      1 MLPG LALLLLA AWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
        |||
Db      1 MLPG LALLLLA AWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
        |||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEE SDNVDSADA EEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
        |||
Db    181 GVEFVCCPLAEE SDNVDSADA EEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDEDGDEVEEEEA EEPYEEATER TTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
        |||
Db    241 EADDDDEDEDGDEVEEEEA EEPYEEATER TTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWE EAERQAKNLPKADKKAVIQHF 360
        |||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWE EAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAA NERQQLVETHMARVEAMLNDRRRLALENYITALQAVPPRPRHVFNMLK 420
        |||
Db    361 QEKVESLEQEAA NERQQLVETHMARVEAMLNDRRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
        |||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy    481 EEIQDEVD ELLQKEQNYSDDLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL 540
        |||
Db    481 EEIQDEVD ELLQKEQNYSDDLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL 540

Qy    541 DDIQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600
```



```

          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      541 DDLQPWHSFGADSVPA NTENEVEPVDARPAAD RGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy      601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIH HGV 660
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIH HGV 660

Qy      661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNK 697
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNK 697

```

RESULT 7

```

US-09-548-372D-18
; Sequence 18, Application US/09548372D
; Patent No. 6420534
; GENERAL INFORMATION:
; APPLICANT: GURNEY ET AL.
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR
AND USES
; TITLE OF INVENTION: THEREOF
; FILE REFERENCE: 29915/6280I
; CURRENT APPLICATION NUMBER: US/09/548,372D
; CURRENT FILING DATE: 2000-04-12
; PRIOR APPLICATION NUMBER: US 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 18
; LENGTH: 697
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-548-372D-18

```

```

Query Match          99.8%; Score 3643; DB 4; Length 697;
Best Local Similarity 99.7%; Pred. No. 5.7e-266;
Matches 695; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

```

```

Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGR LNMH MNVQNGKWDSDPSG TK 60
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGR LNMH MNVQNGKWDSDPSG TK 60

Qy      61 TCIDTKEGILQY CQEVYP ELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      61 TCIDTKEGILQY CQEVYP ELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy      121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGM LLLPCGIDKFR 180
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGM LLLPCGIDKFR 180

Qy      181 GVEFVCCPLAEESDNVDSADAEEDDSVWVG GADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

```

Db	181		GVFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEE	240
Qy	241		EADDEDEDEGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241		EADDEDEDEGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301		DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301		DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361		QEKVESLEQEAAANERQQIVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361		QEKVESLEQEAAANERQQIVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421		KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPVA	480
Db	421		KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPVA	480
Qy	481		EEIQDEVDELLOKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFS	540
Db	481		EEIQDEVDELLOKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFS	540
Qy	541		DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541		DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD	600
Qy	601		RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIH	660
Db	601		RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIH	660
Qy	661		VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697
Db	661		VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697

RESULT 8  
 US-09-548-367D-18  
 ; Sequence 18, Application US/09548367D  
 ; Patent No. 6440698  
 ; GENERAL INFORMATION:  
 ; APPLICANT: GURNEY ET AL.  
 ; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR  
 AND USES  
 ; TITLE OF INVENTION: THEREOF  
 ; FILE REFERENCE: 29915/6280H  
 ; CURRENT APPLICATION NUMBER: US/09/548,367D  
 ; CURRENT FILING DATE: 2000-04-12  
 ; PRIOR APPLICATION NUMBER: US 60/155,493  
 ; PRIOR FILING DATE: 1999-09-23  
 ; PRIOR APPLICATION NUMBER: US 09/404,133  
 ; PRIOR FILING DATE: 1999-09-23  
 ; PRIOR APPLICATION NUMBER: PCT/US99/20881  
 ; PRIOR FILING DATE: 1999-09-23  
 ; PRIOR APPLICATION NUMBER: US 60/101,594  
 ; PRIOR FILING DATE: 1998-09-24  
 ; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn version 3.1  
; SEQ ID NO 18  
; LENGTH: 697  
; TYPE: PRT  
; ORGANISM: Homo sapiens  
US-09-548-367D-18

Query Match 99.8%; Score 3643; DB 4; Length 697;  
Best Local Similarity 99.7%; Pred. No. 5.7e-266;  
Matches 695; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

```
Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDSPSGTK 60
        |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDSPSGTK 60

Qy     61 TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
        |||
Db     61 TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVDPKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |||
Db    121 EFVSDALLVDPKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDDSDVWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
        |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDDSDVWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV 300
        |||
Db    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360
        |||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRRLALENYITALQAVPPRPRHVFNMLK 420
        |||
Db    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
        |||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy    481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSLTETKTTVELLPVNGEFSL 540
        |||
Db    481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSLTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600
        |||
Db    541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDAEF 600

Qy    601 RHDSGYEVHHQKLFFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGHV 660
        |||
Db    601 RHDSGYEVHHQKLFFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGHV 660

Qy    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697
        |||
```

Db 661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMQNKK 697

RESULT 9

US-09-551-853D-18

; Sequence 18, Application US/09551853D

; Patent No. 6500667

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR AND USES

; TITLE OF INVENTION: THEREOF

; FILE REFERENCE: 29915/6280L

; CURRENT APPLICATION NUMBER: US/09/551,853D

; CURRENT FILING DATE: 2000-04-18

; PRIOR APPLICATION NUMBER: US 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn version 3.1

; SEQ ID NO 18

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-551-853D-18

Query Match 99.8%; Score 3643; DB 4; Length 697;

Best Local Similarity 99.7%; Pred. No. 5.7e-266;

Matches 695; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

```
Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGK 60
          |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
          |||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
          |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
          |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDDEDGDEVEEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
          |||
Db    241 EADDDDEDDDEDGDEVEEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360
          |||
```

Accession	Query	Target	Score	E-value
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360	
Qy	361	QEKVESLEQEAAENERQQIVETHMARVEAMLNDRRLALENYITALQAVPPRRPHVFNMLK	420	
Db	361	QEKVESLEQEAAENERQQIVETHMARVEAMLNDRRLALENYITALQAVPPRRPHVFNMLK	420	
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPVA	480	
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPVA	480	
Qy	481	EEIQDEVDELLQKEQNYSDDLANMISEPRISYGN DALMPSLTETKTTVELLPVNGEFS	540	
Db	481	EEIQDEVDELLQKEQNYSDDLANMISEPRISYGN DALMPSLTETKTTVELLPVNGEFS	540	
Qy	541	DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600	
Db	541	DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDAEF	600	
Qy	601	RHDSGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660	
Db	601	RHDSGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660	
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK	697	
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK	697	

```

; CLASSIFICATION: 435
; ATTORNEY/AGENT INFORMATION:
; NAME: Pabst, Patrea L.
; REGISTRATION NUMBER: 31,284
; REFERENCE/DOCKET NUMBER: TSI121
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: (404)-873-8794
; TELEFAX: (404)-873-8795
; INFORMATION FOR SEQ ID NO: 2:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 695 amino acids
; TYPE: amino acid
; TOPOLOGY: linear
; MOLECULE TYPE: protein
US-08-123-702-2

```

```

Query Match          99.7%; Score 3641; DB 1; Length 695;
Best Local Similarity 100.0%; Pred. No. 8e-266;
Matches 695; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```

```

Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
      |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
      |||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
      |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
      |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
      |||
Db    241 EADDDDEDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360
      |||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAAANERQQVLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
      |||
Db    361 QEKVESLEQEAAANERQQVLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
      |||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy    481 EEIQDEVDELLQKEQNYSDDLANMISEPRISYGNDAIMPSTLTETKTTVELLPVNGEFSL 540
      |||
Db    481 EEIQDEVDELLQKEQNYSDDLANMISEPRISYGNDAIMPSTLTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

```

```

Db      541 DDLQPWHSFGADSVPA NTENEVEPVDARPAADRGLTRPGSGLTNIKTEEISEVKMDAEF 600
Qy      601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV 660
Db      601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV 660
Qy      661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
Db      661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695

```

RESULT 11

US-08-104-165-1

; Sequence 1, Application US/08104165

; Patent No. 5877015

; GENERAL INFORMATION:

; APPLICANT: HARDY, John Anthony

; APPLICANT: GOATE, Alison Mary

; APPLICANT: MULLAN, Michael John

; APPLICANT: CHARTIER-HARLIN, Marie-Christine

; APPLICANT: OWEN, Michael John

; TITLE OF INVENTION: Test and Model for Alzheimer's Disease

; NUMBER OF SEQUENCES: 44

; CORRESPONDENCE ADDRESS:

; ADDRESSEE: Townsend and Townsend Khourie and Crew

; STREET: 379 Lytton Avenue

; CITY: Palo Alto

; STATE: California

; COUNTRY: US

; ZIP: 94301

; COMPUTER READABLE FORM:

; MEDIUM TYPE: Floppy Disk

; COMPUTER: IBM PC compatible

; OPERATING SYSTEM: PC-DOS/MS-DOS

; CURRENT APPLICATION DATA:

; APPLICATION NUMBER: US/08/104,165

; FILING DATE: 21-JAN-1992

; CLASSIFICATION: 435

; PRIOR APPLICATION DATA:

; APPLICATION NUMBER: 9101307.8

; FILING DATE: 21-JAN-1991

; APPLICATION NUMBER: 9118445.7

; FILING DATE: 28-AUG-1991

; ATTORNEY/AGENT INFORMATION:

; NAME: Liebeschuetz, Joe

; REGISTRATION NUMBER: 37,505

; REFERENCE/DOCKET NUMBER: 16163-000100

; TELECOMMUNICATION INFORMATION:

; TELEPHONE: (415) 326-2400

; TELEFAX: (415) 326-2422

; INFORMATION FOR SEQ ID NO: 1:

; SEQUENCE CHARACTERISTICS:

; LENGTH: 695 amino acids

; TYPE: amino acid

; STRANDEDNESS: single

; TOPOLOGY: linear

; MOLECULE TYPE: protein  
US-08-104-165-1

Query Match 99.7%; Score 3641; DB 2; Length 695;  
Best Local Similarity 100.0%; Pred. No. 8e-266;  
Matches 695; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Qy	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLOKEQNYSDDLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLOKEQNYSDDLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMMLKKKQYTSIHHGV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMMLKKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	695
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	695

RESULT 12





Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Qy	241	EADDDDEDDEDGDEVEEEAEEPYEEATERTTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDEDGDEVEEEAEEPYEEATERTTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Qy	481	EEIQDEVDELLQKEQNYSDDLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDDLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGHV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGHV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	695
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	695

RESULT 13

US-08-464-250-1

; Sequence 1, Application US/08464250

; Patent No. 6300540

; GENERAL INFORMATION:

; APPLICANT: HARDY, John Anthony

; GOATE, Alison Mary

; MULLAN, Michael John

; CHARTIER-HARLIN, Marie-Christine

; OWEN, Michael John

; TITLE OF INVENTION: Test and Model for Alzheimer's Disease

; NUMBER OF SEQUENCES: 44

```

;   CORRESPONDENCE ADDRESS:
;   ADDRESSEE: Townsend and Townsend Khourie and Crew
;   STREET: 379 Lytton Avenue
;   CITY: Palo Alto
;   STATE: California
;   COUNTRY: US
;   ZIP: 94301
;   COMPUTER READABLE FORM:
;   MEDIUM TYPE: Floppy Disk
;   COMPUTER: IBM PC compatible
;   OPERATING SYSTEM: PC-DOS/MS-DOS
;   CURRENT APPLICATION DATA:
;   APPLICATION NUMBER: US/08/464,250
;   FILING DATE: 05-Jun-1995
;   CLASSIFICATION: 435
;   PRIOR APPLICATION DATA:
;   APPLICATION NUMBER: 08/104,165
;   FILING DATE: 21-JAN-1992
;   APPLICATION NUMBER: 9101307.8
;   FILING DATE: 21-JAN-1991
;   APPLICATION NUMBER: 9118445.7
;   FILING DATE: 28-AUG-1991
;   ATTORNEY/AGENT INFORMATION:
;   NAME: Liebeschuetz, Joe
;   REGISTRATION NUMBER: 37,505
;   REFERENCE/DOCKET NUMBER: 16163-000100
;   TELECOMMUNICATION INFORMATION:
;   TELEPHONE: (415) 326-2400
;   TELEFAX: (415) 326-2422
;   INFORMATION FOR SEQ ID NO: 1:
;   SEQUENCE CHARACTERISTICS:
;   LENGTH: 695 amino acids
;   TYPE: amino acid
;   STRANDEDNESS: single
;   TOPOLOGY: linear
;   MOLECULE TYPE: protein
;   SEQUENCE DESCRIPTION: SEQ ID NO: 1:
US-08-464-250-1

```

Query Match 99.7%; Score 3641; DB 4; Length 695;  
Best Local Similarity 100.0%; Pred. No. 8e-266;  
Matches 695; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

[illegible]

```

Db      181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
Qy      241 EADDDDEDDGDEVEEEAEEPVEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
        |||
Db      241 EADDDDEDDGDEVEEEAEEPVEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
Qy      301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360
        |||
Db      301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360
Qy      361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
        |||
Db      361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
Qy      421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
        |||
Db      421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
Qy      481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540
        |||
Db      481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540
Qy      541 DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600
        |||
Db      541 DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600
Qy      601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGHV 660
        |||
Db      601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGHV 660
Qy      661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
        |||
Db      661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695

```

RESULT 14

US-09-458-481B-7

; Sequence 7, Application US/09458481B

; Patent No. 6310048

; GENERAL INFORMATION:

; APPLICANT: KUMAR, Vijaya B.

; TITLE OF INVENTION: ANTISENSE MODULATION OF AMYLOID BETA PROTEIN EXPRESSION

; FILE REFERENCE: 16153-9250

; CURRENT APPLICATION NUMBER: US/09/458,481B

; CURRENT FILING DATE: 1999-12-09

; NUMBER OF SEQ ID NOS: 20

; SOFTWARE: PatentIn Ver. 2.0

; SEQ ID NO 7

; LENGTH: 695

; TYPE: PRT

; ORGANISM: Monkey

US-09-458-481B-7

Query Match 99.7%; Score 3641; DB 4; Length 695;

Best Local Similarity 100.0%; Pred. No. 8e-266;

Matches 695; Conservative 0; Mismatches 0; Indels 0; Gaps 0;



; CURRENT APPLICATION NUMBER: US/09/458,481B  
; CURRENT FILING DATE: 1999-12-09  
; NUMBER OF SEQ ID NOS: 20  
; SOFTWARE: PatentIn Ver. 2.0  
; SEQ ID NO 8  
; LENGTH: 695  
; TYPE: PRT  
; ORGANISM: Homo sapiens  
US-09-458-481B-8

Query Match 99.7%; Score 3641; DB 4; Length 695;  
Best Local Similarity 100.0%; Pred. No. 8e-266;  
Matches 695; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60
      |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120
      |||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
      |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240
      |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240

Qy    241 EADDDDEDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV 300
      |||
Db    241 EADDDDEDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360
      |||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
      |||
Db    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
      |||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy    481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL 540
      |||
Db    481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSVPAANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600
      |||
Db    541 DDLQPWHSFGADSVPAANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660
      |||
Db    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660
```

|||||

Job time : 17 secs

GenCore version 5.1.6  
Copyright (c) 1993 - 2004 Compugen Ltd.

OM protein - protein search, using sw model

Run on: July 26, 2004, 12:40:23 ; Search time 13.6667 Seconds  
(without alignments)  
4905.768 Million cell updates/sec

Title: US-09-806-194A-16  
Perfect score: 3651  
Sequence: 1 MLPGLALLLLAAWTARALEV.....QQNGYENPTYKFFEQMQNKK 697

Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5

Searched: 283366 seqs, 96191526 residues

Total number of hits satisfying chosen parameters: 283366

Minimum DB seq length: 0  
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

Database : PIR\_78:\*  
1: pir1:\*  
2: pir2:\*  
3: pir3:\*  
4: pir4:\*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	%		DB	ID	Description
		Match	Length			
1	3641	99.7	695	1	A49795	Alzheimer's diseas
2	3590.5	98.3	770	1	QRHUA4	Alzheimer's diseas
3	3544	97.1	695	2	S00550	Alzheimer's diseas
4	3519	96.4	695	2	A27485	Alzheimer's diseas
5	3103	85.0	747	2	JH0773	Alzheimer's diseas
6	2105	57.7	484	4	A32761	hypothetical Alzhe
7	1728	47.3	763	2	A49321	amyloid beta (A4)
8	1716	47.0	765	2	S42880	amyloid precursor-
9	1704	46.7	751	2	A49974	beta-amyloid precu
10	1185	32.5	653	2	A46362	amyloid precursor-
11	1143	31.3	511	2	JC1404	CDEI-box DNA-bindi
12	817.5	22.4	686	2	T15795	hypothetical prote
13	747	20.5	886	2	A32758	beta-amyloid-like



14	706	19.3	246	2	S38344	CDEI-binding prote
15	411	11.3	82	2	PQ0438	Alzheimer's diseas
16	296.5	8.1	191	2	A35981	sperm membrane pro
17	283	7.8	57	2	E60045	Alzheimer's diseas
18	283	7.8	57	2	F60045	Alzheimer's diseas
19	283	7.8	57	2	G60045	Alzheimer's diseas
20	283	7.8	57	2	D60045	Alzheimer's diseas
21	283	7.8	57	2	A60045	Alzheimer's diseas
22	283	7.8	57	2	B60045	Alzheimer's diseas
23	217	5.9	42	2	PN0512	beta-amyloid prote
24	192.5	5.3	1110	2	I51116	NF-180 - sea lampr
25	186	5.1	5170	2	T15348	hypothetical prote
26	185.5	5.1	407	1	EDBEQ3	immediate-early pr
27	185.5	5.1	993	2	S49461	synaptonemal compl
28	182	5.0	522	2	T32444	hypothetical prote
29	175.5	4.8	802	1	S48529	NAB3 protein - yea
30	175.5	4.8	1188	2	T46608	zinc finger protei
31	174.5	4.8	464	2	H90279	microtubule bindin
32	174.5	4.8	884	2	T20405	hypothetical prote
33	174	4.8	579	2	JH0820	160K golgi antigen
34	174	4.8	1087	2	T30330	gelsolin-related p
35	173.5	4.8	793	1	JH0628	caldesmon - human
36	172	4.7	771	1	A33430	h-caldesmon - chic
37	172	4.7	784	2	PN0009	neurofilament trip
38	172	4.7	1182	2	T30189	myelin transcripti
39	171	4.7	1271	2	A45555	glutamate rich pro
40	170	4.7	1948	2	S00485	gene 11-1 protein
41	169.5	4.6	298	1	TPHUTC	troponin T, cardia
42	169.5	4.6	721	2	S29795	hypothetical prote
43	169	4.6	885	2	G71608	ATP-dept. acyl-CoA
44	169	4.6	1187	2	T46637	transcription fact
45	168.5	4.6	675	2	T03744	myoD protein inhib

#### ALIGNMENTS

##### RESULT 1

A49795

Alzheimer's disease amyloid beta protein precursor - crab-eating macaque

C;Species: *Macaca fascicularis* (crab-eating macaque)

C;Date: 10-Sep-1999 #sequence\_revision 10-Sep-1999 #text\_change 10-Sep-1999

C;Accession: A49795

R;Podlisny, M.B.; Tolan, D.R.; Selkoe, D.J.

Am. J. Pathol. 138, 1423-1435, 1991

A;Title: Homology of the amyloid beta protein precursor in monkey and human supports a primate model for beta amyloidosis in Alzheimer's disease.

A;Reference number: A49795; MUID:91273117; PMID:1905108

A;Accession: A49795

A;Status: preliminary

A;Molecule type: mRNA

A;Residues: 1-695 <POD>

A;Cross-references: GB:M58727; NID:g342062; PIDN:AAA36829.1; PID:g342063

C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

C;Keywords: alternative splicing

Query Match 99.7%; Score 3641; DB 1; Length 695;  
Best Local Similarity 100.0%; Pred. No. 4.2e-184;  
Matches 695; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
        |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYQCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
        |||
Db     61 TCIDTKEGILQYQCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
        |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDDEDGDEVEEEAEOPYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
        |||
Db    241 EADDDDEDDDEDGDEVEEEAEOPYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360
        |||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAAANERQQVLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVENMLK 420
        |||
Db    361 QEKVESLEQEAAANERQQVLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVENMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
        |||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy    481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL 540
        |||
Db    481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600
        |||
Db    541 DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV 660
        |||
Db    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV 660

Qy    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
        |||
Db    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
```

RESULT 2

QRHUA4

Alzheimer's disease amyloid beta protein precursor [validated] - human

N;Alternate names: Alzheimer's disease amyloid A4 protein; coagulation factor XIa inhibitor; proteinase nexin II (PN-II)

N;Contains: amyloid beta protein long, plaque form; amyloid beta protein short, vascular form; amyloid protein precursor splice form APP(695); amyloid protein precursor splice form APP(751); amyloid protein precursor splice form APP(770)

C;Species: Homo sapiens (man)

C;Date: 30-Jun-1987 #sequence\_revision 28-Jul-1995 #text\_change 15-Sep-2000

C;Accession: S02260; S05194; A32277; A33260; A35486; I39452; I39451; I39453; I59562; A44017; B44017; A03134; A29030; A47584; A47585; S02638; S00707; S00925; A38949; A30320; B30320; C30320; A31087; A24668; A28583; A29302; A60805; JL0038; S06121; A60355; A59011; A38384; S29076; S38252; S32539; S48148; S48692; S51186; S51185; S51184; S51183; A54238; I58075; I52250; S09010; S10737; S24127; S43644

R;Lemaire, H.G.; Salbaum, J.M.; Multhaup, G.; Kang, J.; Bayney, R.M.; Unterbeck, A.; Beyreuther, K.; Mueller-Hill, B.  
Nucleic Acids Res. 17, 517-522, 1989

A;Title: The PreA4(695) precursor protein of Alzheimer's disease A4 amyloid is encoded by 16 exons.

A;Reference number: S02260; MUID:89128427; PMID:2783775

A;Accession: S02260

A;Molecule type: DNA

A;Residues: 1-288,'V',365-770 <LEM1>

A;Cross-references: EMBL:X13466

A;Note: alternative splice form APP(695)

R;Lemaire, H.G.  
submitted to the EMBL Data Library, November 1988

A;Reference number: S05194

A;Accession: S05194

A;Molecule type: DNA

A;Residues: 1-14,'VW',17-288,'V',365-770 <LEM2>

A;Cross-references: EMBL:X13466; NID:g35598; PIDN:CAA31830.1; PID:g871360

A;Note: alternative splice form APP(695)

R;La Fauci, G.; Lahiri, D.K.; Salton, S.R.J.; Robakis, N.K.  
Biochem. Biophys. Res. Commun. 159, 297-304, 1989

A;Title: Characterization of the 5'-end region and the first two exons of the beta-protein precursor gene.

A;Reference number: A32277; MUID:89165870; PMID:2538123

A;Accession: A32277

A;Molecule type: DNA

A;Residues: 1-75 <LAF>

A;Cross-references: GB:M24546; GB:M24547; NID:g341202; PIDN:AAC13654.1; PID:g516074

R;Johnstone, E.M.; Chaney, M.O.; Moore, R.E.; Ward, K.E.; Norris, F.H.; Little, S.P.  
Biochem. Biophys. Res. Commun. 163, 1248-1255, 1989

A;Title: Alzheimer's disease amyloid peptide is encoded by two exons and shows similarity to soybean trypsin inhibitor.

A;Reference number: A33260; MUID:89392030; PMID:2675837

A;Accession: A33260

A;Molecule type: DNA

A;Residues: 656-737 <JOH>

A;Cross-references: GB:M29270; NID:g178863; PIDN:AAA51768.1; PID:g178865

R;Prelli, F.; Levy, E.; van Duinen, S.G.; Bots, G.T.A.M.; Luyendijk, W.; Frangione, B.  
Biochem. Biophys. Res. Commun. 170, 301-307, 1990

A;Title: Expression of a normal and variant Alzheimer's beta-protein gene in amyloid of hereditary cerebral hemorrhage, Dutch type: DNA and protein diagnostic assays.

A;Reference number: A35486; MUID:90321244; PMID:2196878  
 A;Accession: A35486  
 A;Molecule type: DNA  
 A;Residues: 672-710 <PRE1>  
 A;Note: 693-Gln was found in DNA isolated from HCHWA-D patients  
 R;Yoshikai, S.I.; Sasaki, H.; Doh-ura, K.; Furuya, H.; Sakaki, Y.  
 Gene 87, 257-263, 1990  
 A;Title: Genomic organization of the human amyloid beta-protein precursor gene.  
 A;Reference number: I39451; MUID:90236318; PMID:2110105  
 A;Accession: I39452  
 A;Status: nucleic acid sequence not shown; translation not shown; translated  
 from GB/EMBL/DDBJ  
 A;Molecule type: DNA  
 A;Residues: 1-770 <YOS1>  
 A;Cross-references: GB:M33112; NID:g178613; PIDN:AAB59502.1; PID:g178616  
 A;Accession: I39451  
 A;Status: nucleic acid sequence not shown; translation not shown; translated  
 from GB/EMBL/DDBJ  
 A;Molecule type: DNA  
 A;Residues: 1-530, 'QWLMPVIPAFWEAKVGR' <YOS2>  
 A;Cross-references: GB:M34875; NID:g178608; PIDN:AAB59501.1; PID:g178615  
 R;Yoshikai, S.I.; Sasaki, H.; Doh-ura, K.; Furuya, H.; Sakaki, Y.  
 Gene 102, 291-292, 1991  
 A;Reference number: A59020; MUID:91340168; PMID:1908403  
 A;Contents: annotation; erratum  
 A;Note: revised physical map for reference I39451  
 R;Levy, E.; Carman, M.D.; Fernandez-Madrid, I.J.; Power, M.D.; Lieberburg, I.;  
 van Duinen, S.G.; Bots, G.T.; Luyendijk, W.; Frangione, B.  
 Science 248, 1124-1126, 1990  
 A;Title: Mutation of the Alzheimer's disease amyloid gene in hereditary cerebral  
 hemorrhage, Dutch type.  
 A;Reference number: I39453; MUID:90260663; PMID:2111584  
 A;Accession: I39453  
 A;Status: translated from GB/EMBL/DDBJ  
 A;Molecule type: DNA  
 A;Residues: 656-737 <LEV>  
 A;Cross-references: GB:M37896; NID:g178618; PIDN:AAA51727.1; PID:g178620  
 A;Note: a mutation with 693-Gln is presented  
 R;Murrell, J.; Farlow, M.; Ghetti, B.; Benson, M.D.  
 Science 254, 97-99, 1991  
 A;Title: A mutation in the amyloid precursor protein associated with hereditary  
 Alzheimer's disease.  
 A;Reference number: I59562; MUID:92022553; PMID:1925564  
 A;Accession: I59562  
 A;Status: translated from GB/EMBL/DDBJ  
 A;Molecule type: DNA  
 A;Residues: 689-716, 'F', 718-737 <MUR>  
 A;Cross-references: GB:S57665; NID:g236720; PIDN:AAB19991.1; PID:g236721  
 R;Kamino, K.; Orr, H.T.; Payami, H.; Wijsman, E.M.; Alonso, M.E.; Pulst, S.M.;  
 Anderson, L.; O'dahl, S.; Nemens, E.; White, J.A.; Sadovnick, A.D.; Ball, M.J.;  
 Kaye, J.; Warren, A.; McInnis, M.; Antonarakis, S.E.; Korenberg, J.R.; Sharma,  
 V.; Kukull, W.; Larson, E.; Heston, L.L.; Martin, G.M.; Bird, T.D.;  
 Schellenberg, G.D.  
 Am. J. Hum. Genet. 51, 998-1014, 1992  
 A;Title: Linkage and mutational analysis of familial Alzheimer disease kindreds  
 for the APP gene region.  
 A;Reference number: A44017; MUID:93035397; PMID:1415269

A;Accession: A44017  
 A;Molecule type: DNA  
 A;Residues: 687-692,'G',694-718 <KAM1>  
 A;Cross-references: GB:S45135; NID:g257377; PIDN:AAB23645.1; PID:g257378  
 A;Experimental source: familial Alzheimer disease family SB  
 A;Note: sequence extracted from NCBI backbone (NCBIP:115374)  
 A;Accession: B44017  
 A;Molecule type: DNA  
 A;Residues: 687-718 <KAM2>  
 A;Cross-references: GB:S45136; NID:g257379; PIDN:AAB23646.1; PID:g257380  
 A;Experimental source: familial Alzheimer disease family LIT  
 A;Note: sequence extracted from NCBI backbone (NCBIP:115376)  
 A;Note: this sequence has a silent mutation  
 R;Kang, J.; Lemaire, H.G.; Unterbeck, A.; Salbaum, J.M.; Masters, C.L.;  
 Grzeschik, K.H.; Multhaup, G.; Beyreuther, K.; Muller-Hill, B.  
 Nature 325, 733-736, 1987  
 A;Title: The precursor of Alzheimer's disease amyloid A4 protein resembles a  
 cell-surface receptor.  
 A;Reference number: A03134; MUID:87144572; PMID:2881207  
 A;Accession: A03134  
 A;Molecule type: mRNA  
 A;Residues: 1-288,'V',365-770 <KAN>  
 A;Cross-references: GB:Y00264; NID:g28525; PIDN:CAA68374.1; PID:g28526  
 A;Note: alternative splice form APP(695)  
 R;Robakis, N.K.; Ramakrishna, N.; Wolfe, G.; Wisniewski, H.M.  
 Proc. Natl. Acad. Sci. U.S.A. 84, 4190-4194, 1987  
 A;Title: Molecular cloning and characterization of a cDNA encoding the  
 cerebrovascular and the neuritic plaque amyloid peptides.  
 A;Reference number: A29030; MUID:87231971; PMID:3035574  
 A;Accession: A29030  
 A;Molecule type: mRNA  
 A;Residues: 284-288,'V',365-646,'E',648-770 <ROB>  
 A;Cross-references: GB:M16765; NID:g178539; PIDN:AAA51722.1; PID:g178540  
 A;Note: the authors translated the codon GAG for residue 647 as Asp  
 R;Goldgaber, D.; Lerman, M.I.; McBride, O.W.; Saffiotti, U.; Gajdusek, D.C.  
 Science 235, 877-880, 1987  
 A;Title: Characterization and chromosomal localization of a cDNA encoding brain  
 amyloid of Alzheimer's disease.  
 A;Reference number: A47584; MUID:87120328; PMID:3810169  
 A;Accession: A47584  
 A;Molecule type: mRNA  
 A;Residues: 674-756,'S',758-770 <GOL>  
 A;Cross-references: GB:M15533; NID:g178706; PIDN:AAA35540.1; PID:g178707  
 A;Experimental source: brain  
 R;Tanzi, R.E.; Gusella, J.F.; Watkins, P.C.; Bruns, G.A.P.; St George-Hyslop,  
 P.; Van Keuren, M.L.; Patterson, D.; Pagan, S.; Kurnit, D.M.; Neve, R.L.  
 Science 235, 880-884, 1987  
 A;Title: Amyloid beta protein gene: cDNA, mRNA distribution, and genetic linkage  
 near the Alzheimer locus.  
 A;Reference number: A47585; MUID:87120329; PMID:2949367  
 A;Accession: A47585  
 A;Molecule type: mRNA  
 A;Residues: 674-703 <TAN1>  
 A;Cross-references: GB:M15532; NID:g177957; PIDN:AAA51564.1; PID:g177958  
 R;Dyrks, T.; Weidemann, A.; Multhaup, G.; Salbaum, J.M.; Lemaire, H.G.; Kang,  
 J.; Mueller-Hill, B.; Masters, C.L.; Beyreuther, K.  
 EMBO J. 7, 949-957, 1988

A;Title: Identification, transmembrane orientation and biogenesis of the amyloid A4 precursor of Alzheimer's disease.  
 A;Reference number: S02638; MUID:88296437; PMID:2900137  
 A;Accession: S02638  
 A;Molecule type: mRNA  
 A;Residues: 672-678 <DYR>  
 R;Tanzi, R.E.; McClatchey, A.I.; Lamperti, E.D.; Villa-Komaroff, L.; Gusella, J.F.; Neve, R.L.  
 Nature 331, 528-530, 1988  
 A;Title: Protease inhibitor domain encoded by an amyloid protein precursor mRNA associated with Alzheimer's disease.  
 A;Reference number: S00707; MUID:88122640; PMID:2893290  
 A;Accession: S00707  
 A;Molecule type: mRNA  
 A;Residues: 286-344,'I',365-366 <TAN2>  
 A;Cross-references: EMBL:X06982; NID:g28817; PIDN:CAA30042.1; PID:g929612  
 A;Experimental source: promyelocytic leukemia cell line HL60  
 A;Note: alternative splice form APP(751)  
 R;Ponte, P.; Gonzalez-DeWhitt, P.; Schilling, J.; Miller, J.; Hsu, D.; Greenberg, B.; Davis, K.; Wallace, W.; Lieberburg, I.; Fuller, F.; Cordell, B.  
 Nature 331, 525-527, 1988  
 A;Title: A new A4 amyloid mRNA contains a domain homologous to serine proteinase inhibitors.  
 A;Reference number: S00925; MUID:88122639; PMID:2893289  
 A;Accession: S00925  
 A;Molecule type: mRNA  
 A;Residues: 1-344,'I',365-770 <PO2>  
 A;Cross-references: GB:X06989; EMBL:Y00297; NID:g28720; PIDN:CAA30050.1; PID:g28721  
 A;Note: alternative splice form APP(751)  
 R;Kitaguchi, N.; Takahashi, Y.; Tokushima, Y.; Shiojiri, S.; Ito, H.  
 Nature 331, 530-532, 1988  
 A;Title: Novel precursor of Alzheimer's disease amyloid protein shows protease inhibitory activity.  
 A;Reference number: A38949; MUID:88122641; PMID:2893291  
 A;Accession: A38949  
 A;Molecule type: mRNA  
 A;Residues: 287-367 <KIT>  
 A;Cross-references: GB:X06981; NID:g28816; PIDN:CAA30041.1; PID:g929611  
 A;Experimental source: glioblastoma cell line  
 A;Note: alternative splice form APP(770)  
 R;Vitek, M.P.; Rasool, C.G.; de Sauvage, F.; Vitek, S.M.; Bartus, R.T.; Beer, B.; Ashton, R.A.; Macq, A.F.; Maloteaux, J.M.; Blume, A.J.; Octave, J.N.  
 Brain Res. Mol. Brain Res. 4, 121-131, 1988  
 A;Title: Absence of mutation in the beta-amyloid cDNAs cloned from the brains of three patients with sporadic Alzheimer's disease.  
 A;Reference number: A30320  
 A;Accession: A30320  
 A;Status: not compared with conceptual translation  
 A;Molecule type: mRNA  
 A;Residues: 284-288,'V',365-770 <VIT1>  
 A;Accession: B30320  
 A;Status: not compared with conceptual translation  
 A;Molecule type: mRNA  
 A;Residues: 122-288,'V',365-770 <VIT2>  
 A;Accession: C30320  
 A;Status: not compared with conceptual translation

A;Molecule type: mRNA  
A;Residues: 606-770 <VIT3>  
R;Zain, S.B.; Salim, M.; Chou, W.G.; Sajdel-Sulkowska, E.M.; Majocha, R.E.; Marotta, C.A.  
Proc. Natl. Acad. Sci. U.S.A. 85, 929-933, 1988  
A;Title: Molecular cloning of amyloid cDNA derived from mRNA of the Alzheimer disease brain: coding and noncoding regions of the fetal precursor mRNA are expressed in the cortex.  
A;Reference number: A31087; MUID:88124954; PMID:2893379  
A;Accession: A31087  
A;Molecule type: mRNA  
A;Residues: 507-770 <ZAI>  
A;Cross-references: GB:M18734; NID:g178572; PIDN:AAA51726.1; PID:g178573  
A;Note: the authors translated the codon GAA for residue 599 as Gly, ACC for residue 603 as Val, GTG for residue 604 as Glu, GAG for residue 605 as Leu, CTT for residue 607 as Pro, CCC for residue 608 as Val, GTG for residue 609 as Asn, AAT for residue 610 as Gly, and GGT for residue 655 as Ser  
A;Note: the cited Genbank accession number, J03594, is not in release 101.0  
R;Masters, C.L.; Multhaup, G.; Simms, G.; Pottgiesser, J.; Martins, R.N.; Beyreuther, K.

Query Match 98.3%; Score 3590.5; DB 1; Length 770;  
Best Local Similarity 90.1%; Pred. No. 2.1e-181;  
Matches 694; Conservative 1; Mismatches 0; Indels 75; Gaps 1;

```

Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGK 60
      |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
      |||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
      |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
      |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEEPVEEATERTTSIATTTTTTTESVEEVVR----- 288
      |||
Db    241 EADDDDEDDEDGDEVEEEAEEPVEEATERTTSIATTTTTTTESVEEVVREVCSEQAETGPC 300

Qy    289 ----- 288

Db    301 RAMISRWFYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMVCGSAMSQSLLKTTQEPLARD 360

Qy    289 ---VPTTAASTPDAVDKYLET PGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQA 345
      :|||
Db    361 PVKLPTTAASTPDAVDKYLET PGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQA 420

Qy    346 KNLPKADKKAVIQHFQEKVESLEQEAAANERQQLVETHMARVEAMLNDRRRLALENYITAL 405
      |||
Db    421 KNLPKADKKAVIQHFQEKVESLEQEAAANERQQLVETHMARVEAMLNDRRRLALENYITAL 480

```

Qy 406 QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER 465  
 |||  
 Db 481 QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER 540

Qy 466 MNQSLSLLYNVPVAEELQDEVDLQKEQNYSDVLANMISEPRISYGNDALMPSLTET 525  
 |||  
 Db 541 MNQSLSLLYNVPVAEELQDEVDLQKEQNYSDVLANMISEPRISYGNDALMPSLTET 600

Qy 526 KTTVELLPVNGEFSDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTN 585  
 |||  
 Db 601 KTTVELLPVNGEFSDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTN 660

Qy 586 IKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITL 645  
 |||  
 Db 661 IKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITL 720

Qy 646 VMLKKKQYTSIHGVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695  
 |||  
 Db 721 VMLKKKQYTSIHGVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 770

# RESULT 3

S00550

Alzheimer's disease amyloid beta protein precursor - rat

N;Alternate names: beta-A4 amyloid protein

C;Species: Rattus norvegicus (Norway rat)

C;Date: 30-Jun-1989 #sequence\_revision 30-Jun-1989 #text\_change 13-Aug-1999

C;Accession: S00550; A41245; A39820; S46251

R;Shivers, B.D.; Hilbich, C.; Multhaup, G.; Salbaum, M.; Beyreuther, K.; Seeburg, P.H.

EMBO J. 7, 1365-1370, 1988

A;Title: Alzheimer's disease amyloidogenic glycoprotein: expression pattern in rat brain suggests a role in cell contact.

A;Reference number: S00550; MUID:88312583; PMID:2900758

A;Accession: S00550

A;Molecule type: mRNA

A;Residues: 1-695 <SHI>

A;Cross-references: EMBL:X07648; NID:g55616; PIDN:CAA30488.1; PID:g55617

R;Schubert, D.; Schroeder, R.; LaCorbiere, M.; Saitoh, T.; Cole, G.

Science 241, 223-226, 1988

A;Title: Amyloid beta protein precursor is possibly a heparan sulfate proteoglycan core protein.

A;Reference number: A41245; MUID:88264430; PMID:2968652

A;Accession: A41245

A;Molecule type: protein

A;Residues: 18-37,'X',39-40,'X',42-44 <SCH>

A;Note: evidence for heparan sulfate attachment

R;Hesse, L.; Beher, D.; Masters, C.L.; Multhaup, G.

FEBS Lett. 349, 109-116, 1994

A;Title: The beta-A4 amyloid precursor protein binding to copper.

A;Reference number: S46251; MUID:94320627; PMID:7913895

A;Contents: annotation; copper binding sites

A;Note: rat peptides were isolated but not sequenced

R;Potempska, A.; Styles, J.; Mehta, P.; Kim, K.S.; Miller, D.L.

J. Biol. Chem. 266, 8464-8469, 1991

A;Title: Purification and tissue level of the beta-amyloid peptide precursor of rat brain.



A;Reference number: A39820; MUID:91217087; PMID:1673681  
A;Accession: A39820  
A;Status: preliminary  
A;Molecule type: protein  
A;Residues: 18-32 <POT>  
A;Experimental source: brain  
C;Comment: Deposition of amyloid protein as neurofibrillary tangles and/or plaques is characteristic of both Alzheimer's disease and Down's syndrome.  
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology  
C;Keywords: alternative splicing; amyloid; glycoprotein; transmembrane protein  
F;625-648/Domain: transmembrane #status predicted <TMM>

Query Match 97.1%; Score 3544; DB 2; Length 695;  
Best Local Similarity 97.3%; Pred. No. 5.3e-179;  
Matches 676; Conservative 7; Mismatches 12; Indels 0; Gaps 0;

```

Qy      1  MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
      ||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      1  MLPSLALLLLAAWTVRALEVPTDGNAGLLAEPQIAMFCGKLNMHMNVQNGKWESDPSGTK 60

Qy     61  TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
      ||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db     61  TCIGTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHTHIVIPYRCLVG 120

Qy    121  EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
      ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    121  EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181  GVEFVCCPLAEESDNVDSADAEEEDSDVWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
      ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    181  GVEFVCCPLAEESDSIDSADAEEEDSDVWGGADTDYADGGEDKVVEVAEEEEVADVEEEE 240

Qy    241  EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
      ||: |||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    241  EAEDDEDVEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301  DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360
      ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    301  DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360

Qy    361  QEKVESLEQEAAERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPHVFNMLK 420
      ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    361  QEKVESLEQEAAERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPHVFNMLK 420

Qy    421  KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480
      ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    421  KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480

Qy    481  EEIQDEVDELLQKEQNYSDDLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL 540
      ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    481  EEIQDEVDELLQKEQNYSDDLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL 540

Qy    541  DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600
      ||||| || ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    541  DDLQPWHFPGVDSVPANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

```

```
Qy      601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVIIATVIVITLVMMLKKKQYTSIHGHV 660  
        ||||:| | ||||||||||||||||||||||||||||||||||||||||  
Db      601 GHDSGFVRHQKLVFFAEDVGSNKGAIIGLMVGGVIIATVIVITLVMMLKKKQYTSIHGHV 660  
  
Qy      661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695  
        ||||||||||||||||||||||||||||  
Db      661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
```

## RESULT 4

A27485  
Alzheimer's disease amyloid beta/A4 protein homolog precursor - mouse  
N;Alternate names: proteinase nexin II  
C;Species: Mus musculus (house mouse)  
C;Date: 31-Mar-1989 #sequence\_revision 31-Mar-1989 #text\_change 13-Aug-1999  
C;Accession: A27485; S19727; I49485  
R;Yamada, T.; Sasaki, H.; Furuya, H.; Miyata, T.; Goto, I.; Sakaki, Y.  
Biochem. Biophys. Res. Commun. 149, 665-671, 1987  
A;Title: Complementary DNA for the mouse homolog of the human amyloid beta  
protein precursor.  
A;Reference number: A27485; MUID:88106489; PMID:3322280  
A;Accession: A27485  
A;Molecule type: mRNA  
A;Residues: 1-695 <YAM>  
A;Cross-references: GB:M18373; NID:g191568; PIDN:AAA37139.1; PID:g309085  
A;Experimental source: brain  
R;de Strooper, B.; van Leuven, F.; van den Berghe, H.  
Biochim. Biophys. Acta 1129, 141-143, 1991  
A;Title: The amyloid beta protein precursor or proteinase nexin II from mouse is  
closer related to its human homolog than previously reported.  
A;Reference number: S19727; MUID:92096458; PMID:1756177  
A;Accession: S19727  
A;Molecule type: mRNA  
A;Residues: 1-210,'G',212-220,'S',222-396,'A',398-402,'T',404-448,'A',450-695  
<STR>  
A;Cross-references: EMBL:X59379  
R;Izumi, R.; Yamada, T.; Yoshikai, S.; Sasaki, H.; Hattori, M.; Sakaki, Y.  
Gene 112, 189-195, 1992  
A;Title: Positive and negative regulatory elements for the expression of the  
Alzheimer's disease amyloid precursor-encoding gene in mouse.  
A;Reference number: I49485; MUID:92209998; PMID:1555768  
A;Accession: I49485  
A;Status: translated from GB/EMBL/DDBJ  
A;Molecule type: DNA  
A;Residues: 1-19 <RES>  
A;Cross-references: GB:D10603; NID:g220328; PIDN:BAA01456.1; PID:g220329  
C;Genetics:  
A;Map position: 16C3  
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type  
proteinase inhibitor homology  
C;Keywords: alternative splicing; amyloid; transmembrane protein

Query Match 96.4%; Score 3519; DB 2; Length 695;  
Best Local Similarity 96.8%; Pred. No. 1.1e-177;  
Matches 673; Conservative 5; Mismatches 17; Indels 0; Gaps 0;

Qy 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRNLNMHMNVQNGKWDSDPSGTK 60



A;Title: A Xenopus homologue of the human beta-amyloid precursor protein: developmental regulation of its gene expression.  
A;Reference number: JH0773; MUID:93129227; PMID:1282805  
A;Accession: JH0773  
A;Molecule type: mRNA  
A;Residues: 1-747 <OKA>  
A;Cross-references: GB:S52417; NID:g263150; PIDN:AAB24853.1; PID:g263151  
A;Experimental source: larva  
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology  
C;Keywords: alternative splicing; amyloid  
F;287-337/Domain: animal Kunitz-type proteinase inhibitor homology <BPI>

Query Match 85.0%; Score 3103; DB 2; Length 747;  
Best Local Similarity 81.0%; Pred. No. 8.8e-156;  
Matches 598; Conservative 35; Mismatches 41; Indels 64; Gaps 5;

```

Qy      17 ALEVPTDGNAGLLAEPQIAMF-CGRLNMHMNVQNGKWSDPSGKTCIDTKEGILQYCQE 75
      |||| ||| ||||||||| |||||||||::| || || |||||||||
Db      15 ALEVLVDGNGGLLAEPQIAMFSVARLNMHMNVQNGKWETDVSG---CIGTKEGILQYCQE 71

Qy      76 VYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVGEFVSDALLVPDKCKF 135
      |||||||||||||||||||||:|||||: | |:|||||||||||||||||||
Db      72 VYPELQITNVVEANQPVTIQNWCKKGRKQCKSRTHIVVPYRCLVGEFVSDALLVPDKCKF 131

Qy     136 LHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEFVCCPLAEESDN 195
      ||||||:|||||||||||:|||| |:|:||||||||||||||||||| |||::
Db     132 LHQERMDICETHLHWHTVAKESCSEKSMLEHYGMLLPCGIDKFRGVEFVCCPSAEES 191

Qy     196 VDSADAAEEDSDVWVGADTDYADGSEDKVVEVA---EEEEVAEVEEEEADDDDEDDEDGDE 253
      ||||| ||| ||||||| || | |:| || || |||| ||||| |||| ||||
Db     192 FDSADAAEEDDCDVWVGADADYVDRSDDKAVEAQPDEEEVVEVEEEEETDDDED--DGDE 249

Qy     254 VEEEAEEPYEEATERTTTSIATTTTTTTTSESVEEVVR----- 288
      ||| |||||||||||||||||||||||||
Db     250 AEEEPPEPYEEATERTTTSIATTTTTTTTSESVEEVVREVCSEQAETGPCRAMISRWYYDVTE 309

Qy     289 -----VPTTAASTPDAVDKYLETPGDENEHAHFQ 317
      :| ||||||||| || |||| |
Db     310 SKCAQFIYGGCGGNRNRFESDDYCMVCGSVIPATAASTPDAVDKYLENPDENEDHDFL 369

Qy     318 KAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHFQEKVESLEQEAAERQQ 377
      ||||| |||:|:|:|:||||||||||||||||||||||| |||
Db     370 KAKERLEGKHREKMEVMKEWEEAERQAKNLPKADKKAVIQHFQEKVESLEQEAAKQRQQ 429

Qy     378 LVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHF 437
      ||||||||||||||||:||||||| |||||||||||||||||||||
Db     430 LVETHMARVEAMLNDRRLALENYITALQADPPRPRHVFNMLKKYVRAEQKDRQHTLKHF 489

Qy     438 EHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVAEEIQDEVDELLQKEQNY 497
      ||||||||||||||||||| ||||| ||| ||||||||||||| |||||
Db     490 EHVRMVDPKKAAQIRSQVMTHLRVINERMNQSFSLLYKVPVAVAEEIQDEVDELFFQKEQNY 549

Qy     498 SDDVLANMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSLDDLQPWHSFGADSV PAN 557
      |||::|:|:| |:|||||||:|||||||:|:|:|:||||||| |||||
Db     550 SDDMVSNMVSDHRVSYGN DALMPSLSETKTTVELLPVDGFEFNIEDLQPWHSFGVDSVPAN 609

```

```

Qy      558 TENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEFRHDSGYEVHHQKLVFFA 617
      |||
Db      610 TENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDSEYRHDTAYEVHHQKLVFFA 669

Qy      618 EDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGVEVDAAVTPEERHLSKM 677
      |:|
Db      670 EEVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTTIHGVEVDAAVTPEERHLTKM 729

Qy      678 QQNGYENPTYKFFEQMQN 695
      |||
Db      730 QQNGYENPTYKFFEQMQN 747

```

# RESULT 6

A32761

hypothetical Alzheimer's disease amyloid beta protein, Alu-containing clone - human (fragment)

C;Species: Homo sapiens (man)

C;Date: 29-Jan-1990 #sequence\_revision 10-Apr-1996 #text\_change 10-Apr-1996

C;Accession: A32761

R;de Sauvage, F.; Octave, J.N.

Science 245, 651-653, 1989

A;Title: A novel mRNA of the A4 amyloid precursor gene coding for a possibly secreted protein.

A;Reference number: A32761; MUID:89346754; PMID:2569763

A;Accession: A32761

A;Molecule type: mRNA

A;Residues: 1-484 <DES>

A;Cross-references: GB:M28373

A;Note: the authors translated the codon ATG for residue 433 as Leu

C;Comment: This is the hypothetical translation of a sequence believed to contain cloning artifacts.

C;Keywords: cloning artifact

```

Query Match          57.7%;  Score 2105;  DB 4;  Length 484;
Best Local Similarity 87.7%;  Pred. No. 1.5e-103;
Matches 407;  Conservative 1;  Mismatches 0;  Indels 56;  Gaps 1;

```

```

Qy      80 LQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVGEFVSDALLVPDKCKFLHQE 139
      |||
Db      1  LQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVGEFVSDALLVPDKCKFLHQE 60

Qy      140 RMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEFVCCPLAEESDNVDSA 199
      |||
Db      61 RMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEFVCCPLAEESDNVDSA 120

Qy      200 DAEEDDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEEADDDDEDDEDGDEVEEEEAE 259
      |||
Db      121 DAEEDDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEEADDDDEDDEDGDEVEEEEAE 180

Qy      260 EPYEEATERTTSIATTTTTTTTESVEEVVR----- 288
      |||
Db      181 EPYEEATERTTSIATTTTTTTTESVEEVVREVCSEQAETGPCRAMISRWFYFDVTEGKCAPF 240

Qy      289 -----VPTTAASTPDAVDKYLETPGDENEHAHFQKAKERL 323
      :|||
Db      241 FYGGCGGNRNNFDTEEYCMAVCGSAIPTTAASTPDAVDKYLETPGDENEHAHFQKAKERL 300

```

Qy 324 EAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHM 383  
 |||  
 Db 301 EAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHM 360  
 Qy 384 ARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMV 443  
 |||  
 Db 361 ARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMV 420  
 Qy 444 DPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAAVEEIQDEV 487  
 |||  
 Db 421 DPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAAVEEIQDEV 464

# RESULT 7

A49321

amyloid beta (A4) homolog 2 precursor - human

N;Alternate names: CDEI-binding protein

C;Species: Homo sapiens (man)

C;Date: 24-Feb-1994 #sequence\_revision 18-Nov-1994 #text\_change 13-Aug-1999

C;Accession: A49321; S34644; S40519

R;Sprecher, C.A.; Grant, F.J.; Grimm, G.; O'Hara, P.J.; Norris, F.; Norris, K.; Foster, D.C.

Biochemistry 32, 4481-4486, 1993

A;Title: Molecular cloning of the cDNA for a human amyloid precursor protein homolog: evidence for a multigene family.

A;Reference number: A49321; MUID:93250009; PMID:8485127

A;Accession: A49321

A;Status: preliminary

A;Molecule type: mRNA

A;Residues: 1-763 <SPR>

A;Cross-references: GB:S60099; NID:g300168; PIDN:AAC60589.1; PID:g300169

A;Experimental source: placenta

A;Note: sequence extracted from NCBI backbone (NCBIN:131198, NCBIP:131199)

A;Note: expression was shown in placenta, brain, heart, lung, liver, and kidney

R;von der Kammer, H.; Klaudiny, J.; Hanes, J.; Scheit, K.H.

submitted to the EMBL Data Library, April 1993

A;Description: The human homologue of the murine CDEI binding protein is an amyloid precursor like protein.

A;Reference number: S34644

A;Accession: S34644

A;Molecule type: mRNA

A;Residues: 1-763 <VON>

A;Cross-references: EMBL:Z22572; NID:g394763; PIDN:CAA80295.1; PID:g394764

R;Wasco, W.; Gurubhagavatula, S.; Paradis, M.; Romano, D.M.; Sisodia, S.S.;

Hyman, B.T.; Neve, R.L.; Tanzi, R.E.

Nature Genet. 5, 95-99, 1993

A;Title: Isolation and characterization of APLP2 encoding a homologue of the Alzheimer's associated amyloid beta protein precursor.

A;Reference number: S40519; MUID:94035131; PMID:8220435

A;Accession: S40519

A;Status: preliminary

A;Molecule type: mRNA

A;Residues: 1-763 <WAS>

A;Cross-references: GB:L27631; NID:g450391; PIDN:AAC41701.1; PID:g450392

C;Genetics:

A;Gene: GDB:APLP2; APPL2

A;Cross-references: GDB:139159; OMIM:104776  
A;Map position: 11q23-11q25  
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type  
proteinase inhibitor homology  
C;Keywords: alternative splicing; transmembrane protein  
F;310-360/Domain: animal Kunitz-type proteinase inhibitor homology <BPI>

Query Match 47.3%; Score 1728; DB 2; Length 763;  
Best Local Similarity 47.1%; Pred. No. 1.7e-83;  
Matches 372; Conservative 112; Mismatches 165; Indels 140; Gaps 20;

```

Qy      5 LALLLLAAWTARALEV-----PTDGNAG---LLAEPQIAMFCGRRLNMHMNVQNGKWDSDP 56
      | | | | | | | | | | : | | | | | | | | | | : | | | | | | | | | | : | | | | |
Db     15 LLLLLLVGLTAPALALAGYIEALANAGTGFAVAEPQIAMFCGKLNMHVNIQTGKWEPPD 74

Qy     57 SGTKTCTIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYR 116
      : | | | : | | | : | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db     75 TGTKSCFETKEEVLYCQEMYPELQITNVMEANQRVSDNWCRRDKKQCKS--RFVTPFK 132

Qy    117 CLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGI 176
      | | | | | | | | | | : | | | : | | | | | | | | | | | | | | | | | | | |
Db    133 CLVGEFVSDVLLVPEKCQFFHKERMEVCENHQHWHTVVKEACLTQGMTLYSYGMLLPCGV 192

Qy    177 DKFRGVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAE 236
      | : | | | : | | | : | | | : | | | : | | | : | | | : | | | : | | |
Db    193 DQFHGTEYVCCPQTKIIGSVSKEEEEEDEE-----EEEEDEEEDYDVYKSEFPTEAD 245

Qy    237 VEE--EEA--DDDEDDDEDGDEVEEEAEOPY-----EEATERTTSIATTTTTTTT 282
      : | : | | : | | | : | | | : | | | : | | | : | | | : | | | : | | |
Db    246 LEDFTEAAVDEDEDEEEGEEVVEDRDYYYDTFKGDDYNEENPTEPGSDGTMSDKEITHD 305

Qy    283 VEEV-----VRVP 290
      | : | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db    306 VKAVCSQEAMTGPCRAVMPRWYFDLSKGKCVRFYGGCGGNRNNFESEDYCMVCKAMIP 365

Qy    291 TTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPK 350
      | | | | | | | | | | : | | | | | | | | | | : | | | | | | | | | | |
Db    366 PTPLPTND-VDVYFETSADDNEHARFQKAKEQLEIRHRNRMDRVKKEWEEAELQAKNLPK 424

Qy    351 ADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPP 410
      | : : : | | | | | : | | | : | | | : | | | : | | | : | | | : | | |
Db    425 AERQTLIQHFQAMVKALEKEAASEKQQLVETHLARVEAMLNDRRRMALENYLAALQSDPP 484

Qy    411 RPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQL 470
      | | : | | : | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db    485 RPHRILQALRRYVRAENKDRLHTIRHYQHVLAVDPEKAAQMKSQVMTHLHVIEERNQL 544

Qy    471 SLLYNVPAVAEEIQDEVDELLQKEQNYSDDLANMISEPRISYGNDALMPSLTETKTTVE 530
      | | | | | | | | | | : | | | : | | | : | | | : | | | : | | | : | | |
Db    545 SLLYKVPYVAQEIQEEIDELLQEQR-----ADM-----DQFTASISETPVDVR 587

Qy    531 LLPVNGEFSDDLQPDWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTN----- 585
      | : | | : : | : | | | | | | | | | | : | | : : | | | : | | |
Db    588 ---VSSEES-EEIPPFHPF--HPFPALPENE---DTQPELYHPM--KKGSGVGEQDGGL 635

Qy    586 IKTEE---ISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGS-----NKG 625
      | | | | | | | | | | : | | : : : | | | | | | | | | | | | | | | |

```

Db	636 IGAEKVINSKNKVDENMVIDETLDV--KEMIFNAERVGGLEERESVGPLREDFSLSSS	693
QY	626 AIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGVEVDAAVTPEERHLSKMQQNGYENP	685
	:     :             :       :     :       :           :	
Db	694 ALIGLLVIAVAIATVIVISILVMLRKRQYGTISHGIVEVDPMLTPEERHLNKMQNHYENP	753
QY	686 TYKFFEQMQ	694
	:	
Db	754 TYKYLEQMQ	762

Query Match 47.0%; Score 1716; DB 2; Length 765;  
Best Local Similarity 46.2%; Pred. No. 7.4e-83;  
Matches 364; Conservative 122; Mismatches 166; Indels 136; Gaps 20;



Db	133	CLVGEFVS	DVLLVPENCQFFHQERMEVCEKHQRWHTVVKEACLTEGMTLYSYGMLLPCGV	192			
Qy	177	DKFRGVEFVCCPLAE--ESDNVDSADAAEEDSDSVWWGGADTDYA-DGSEDKVVEVAEEEE	233				
Db	193	DQFHGT	EYVCCPQT	KVVDSDSTMSKEEEEEEEEEE---DEEDYALDKSEFPTEADLEDFT	248		
Qy	234	VAEVEEEEEADDDEDDEDGDEVEEEEAEPYEE-----ATERTTSIATTTTTTTTESVVEEVV	287				
Db	249	EEAAADEDEDEEEEEEEEEEGEEVVEDRDYYYDSFKGDYNEENPTPESSDGTISDKEIAHDV	308				
Qy	288	R-----	-----VPT	291			
Db	309	KAVCSQEAMTGPCRAVM	PRWYFDLSKGKCVRFIYGCGGNRRNFESEDYCM	AVCKTMIPP	368		
Qy	292	TAASTPD	AVDKYLETPGDENEHAHFQAKAKERLEAKHRERMSQVMREWEAERQAKNLPKA	351			
Db	369	TPLPTND-VDVYFETS	SADDNEHARFQKAKEQLEIRHSRMDRVKKEWEEAELQAKNLPKA	427			
Qy	352	DKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPR	411				
Db	428	ERQTLIQHFQAMVKALEKEAASEKQQLVETHLARVEAMLNDRRLALENYLAALQSDPPR	487				
Qy	412	PRHVFNM	LKKYVRAEQKDRQHTLKHFEHV	RMVDPKKAQIRSQVMTHLRVIYERMNQSL	471		
Db	488	PHRILQALRRYVRAENKDRLHTIRHYQHVLAVDPEKAAQMKSQVMTHLHVIEERNQSL	547				
Qy	472	LLYNVPAVAEEIQDEVDELLOKEQNYSDDLANMISEPRISYGNDALMPSLTETKTVEL	531				
Db	548	LLYKV	PYYAQEIQEIDELLQEQR-----ADM-----DQFTSSISENPVDVR-	589			
Qy	532	LPVNGEFSLDDLQPWHSFGADSV	PANTENEVEPVDPARPAADRGLTTRPGSGLTN-----I	586			
Db	590	--VSSEES-EEIPPFHPF--HPFPS	LSENE---DTQPELYHPM--KKGSGMAEQDGGLI	638			
Qy	587	KTEE---	I SEVKMDAEFRHDSGYEVHHQKL	VFFAEDVGS-----NKGA	626		
Db	639	GAE	EKVINSKNKM	DENMVIDETLDV--KEMI FNAERVGGLEE	EPDSVGPLREDFSLS	SSSA	696
Qy	627	IIGLMVGGVVIATVIVITL	VMLKKKQYTSIH	HGVVEVDAAVTPEERHL	SKMQONGYENPT	686	
Db	697	LIGLLVIAVAIATVIVISL	VMLRKRYGTISHGIVEVH	PMLTPEERHLNKM	QNHN	GYENPT	756
Qy	687	YKF	FSEQMQ	694			
Db	757	YK	LEYMQ	764			

## RESULT 9

beta-amyloid precursor protein 2 homolog APLP2 - mouse

C;Date: 06-Oct-1994 #sequence revision 18-Nov-1994 #text change 13-Aug-1999

R;Slunt, H.H.; Thinakaran, G.; Von Koch, C.; Lo, A.C.; Tanzi, R.E.; Sisodia, S.S.

A;Title: Expression of a ubiquitous, cross-reactive homologue of the mouse beta-amyloid precursor protein (APP).  
A;Reference number: A49974; MUID:94132029; PMID:8300594  
A;Accession: A49974  
A;Status: preliminary; not compared with conceptual translation  
A;Molecule type: nucleic acid  
A;Residues: 1-751 <SLU>  
A;Cross-references: GB:U15571; NID:g558467; PIDN:AAA50603.1; PID:g558468  
A;Note: sequence extracted from NCBI backbone (NCBIP:144636)  
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology  
F;310-360/Domain: animal Kunitz-type proteinase inhibitor homology <BPI>

Query Match 46.7%; Score 1704; DB 2; Length 751;  
Best Local Similarity 45.9%; Pred. No. 3.1e-82;  
Matches 363; Conservative 113; Mismatches 159; Indels 156; Gaps 20;

```
Qy      5 LALLLLAAWTARALEV-----PTDGNAG---LLAEPQIAMFCGRLNMHMNVQNGKWSDP 56
      | :||| || | : ||| :||| ||||| :||| :| | ||| : ||
Db     15 LLVLLLLGLTAPAAALAGYIEALAANAGTGFVAEAPQIAMFCGKLMHVNIQTGWEPDP 74

Qy     57 SGTKTCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYR 116
      :||| :| ||| :||| ||| :||| ||| :||| ||| :| ||| :|
Db     75 TGTKSCLGTKEEVLQYCQEIYPELQITNVMEANQPVNIDSWCRRDKRQCKS--HIVIPFK 132

Qy    117 CLVGEFVSDALLVDPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGI 176
      ||||| |||| | :| |||| :|| | ||| : || | : | : ||||| :
Db    133 CLVGEFVSDVLLVPDNCQFFHQERMEVCEKHQRWHTLVKEACLTEGLTLYSYGMLLPCGV 192

Qy    177 DKFRGVEFVCCPLAE--ESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAE---E 231
      | :| | | :||| : :||| | : ||| : | | || : : :| |
Db    193 DQFHGTEYVCCPQTKTVDSSTMSKEEEEEEE-----DEEDEEEDYDLKSEFPTE 243

Qy    232 EEVAEVEEEEEAD-DEDEDGDEVEEE-----AEPYEEATERTTSIATTT 276
      : : : | || :||| :||| :| : | | | :| | |
Db    244 ADLEDFTAAADEEEEEDEEGEEVVEDRDYYDPFKGDDYNEENPTEPSSEGTTIS----- 298

Qy    277 TTTTESVEEV----- 286
      | | :|
Db    299 --DKEIVHDVKAVCSQEAMTGPCRAVMRWYFDLSKGKCVRFIYGGCGGNRNFESEDYC 356

Qy    287 -----VRVPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEA 341
      :| | | | | | | | | | | | | | | | | | | | | | | | | |
Db    357 MAVCKAMIPPTPLPTND-VDVYFETSADDNEHARFQKAKEQLEIRHRNRMDRVKKEWEA 415

Qy    342 ERQAKNLPKADKKAVIQHFQEKVESLEQEAANERQQQLVETHMARVEAMLNDRRRIALENY 401
      | ||||| : : : |||| | :||| :||| :||| :||| :||| :|||
Db    416 ELQAKNLPKTERQTLIQHFQAMVKALEKEAASEKQQLVETHLARVEAMLNDRRRIALENY 475

Qy    402 ITALQAVPPRPRHVFENMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRV 461
      : ||| : |||| : | :||| || | ||| :||| :||| :||| :|||
Db    476 LAALQSDPPRPHRILQALRRYVRAENKDRLHTIRHYQHVLAVDPEKAAQMKSQVMTHLHV 535

Qy    462 IYERMNQSLSLLYNVPAVAEEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPS 521
      | || ||||| || ||| :||| :||| :||| :||| :||| :|||
Db    536 IEERRNQSLSLLYKVPYVAQEIQEEIDELLQEQR-----ADM-----DQFTSS 578
```

```

Qy      522 LTETKTTVELLPVNGEFSLDDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGS 581
      ::| | : | : | | | | : : || | : : |
Db      579 ISENPDVDRVSSEESE-EIPPFHPLHPF-----PSLSENE-----GSGMAEQDG- 621

Qy      582 GLTNIKTEEI-SEVKMDAEFRHDSGYEVHHQKLVFFAEDVGS-----N 623
      || : : | | : || | : | : : : | || || :
Db      622 GLIGAEKVIN SKNKM DENMVIDETLDV--KEMIFNAERVGGLEEEEPESVGPLREDFSL 679

Qy      624 KGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGVVEVDAAVTPEERHLSKMQQNGYE 683
      | : || : | | || || || : || || : | || : || | : || || : || |
Db      680 SNALIGLLVIAVAIATVIVISLVMLRKRQYGTISHGIVEVDPMLTPEERHLNKMQNHYGE 739

Qy      684 NPTYKFFEQMQ 694
      |||| : |||
Db      740 NPTYKYLEQMQ 750

```

# RESULT 10

A46362

amyloid precursor-like protein - mouse

C;Species: Mus musculus (house mouse)

C;Date: 21-Sep-1993 #sequence\_revision 18-Nov-1994 #text\_change 24-Nov-1999

C;Accession: A46362

R;Wasco, W.; Bupp, K.; Magendantz, M.; Gusella, J.F.; Tanzi, R.E.; Solomon, F.  
Proc. Natl. Acad. Sci. U.S.A. 89, 10758-10762, 1992

A;Title: Identification of a mouse brain cDNA that encodes a protein related to  
the Alzheimer disease-associated amyloid beta protein precursor.

A;Reference number: A46362; MUID:93066322; PMID:1279693

A;Accession: A46362

A;Status: preliminary

A;Molecule type: nucleic acid

A;Residues: 1-653 <WAS>

A;Experimental source: brain

A;Note: sequence inconsistent with the nucleotide translation

A;Note: sequence extracted from NCBI backbone (NCBIN:118683, NCBIP:118684)

C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type  
proteinase inhibitor homology

C;Keywords: transmembrane protein

```

Query Match          32.5%;  Score 1185;  DB 2;  Length 653;
Best Local Similarity 38.6%;  Pred. No. 5e-55;
Matches 270;  Conservative 121;  Mismatches 231;  Indels 78;  Gaps 17;

```

```

Qy      1  MLPGLALLLLAAWTARA-LEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGT 59
      :|| | : || | | | | | | : | | : | | | | : | : : | : | : | :
Db      22  LLP-LSLLLLRAQLAVGNLAVGSPSAAEAPGSAQVAGLCGRLTLHRDLRTGRWEPDPQRS 80

Qy      60  KTCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHF-VIPYRCL 118
      : | : : : | : : : : || | | : | : : || | | | : | : |
Db      81  RRCLLDLPQRVLEYCRQMYPELHIA RVEQAAQAI PMERWCGGTRSGRCAHPHHEVVPFHCL 140

Qy      119 VGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDK 178
      |||| : |||| : | : || || || || : | | : || || || || :
Db      141 PGEFVSEALLVPEGCRFLHQERMDQCESSTRRHQEAQEAQACSSQGLILHGSGMLLPCGSDR 200

Qy      179 FRGVEFVCCPLAEESDNVDSADAEEDDSVDW-WGGADTDYADGSEDKVVEVAEEEEVAEV 237
      |||| : || | : | : : | || | : | || | || |

```

```

Db      201 FRGVEYVCCP-PPATPNPSGMAAGDPSTRSWPLGGR----AEGGED-----EEEVESF 248
Qy      238 EEEEADDEDEDEDGDEVEEEAEFPYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASP 297
      : | : :| ||| || : | : : | | ||
Db      249 PQPVDDYFVEPPQAEEEEEEEEERAPPPSSHTPVMVSRVTPTPR-----PT----- 294
Qy      298 DAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVI 357
      | || | ||: || | :|| || : :::||| | : |:|||||:::|:
Db      295 DGVDVYFGMPGEIGEHEGFLRAKMDLEERRMRQINEVMREWAMADSQSKNLPKADRQALN 354
Qy      358 QHFQEKVESLEQEAAERQQIVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFN 417
      :||| :::|::: : |||:|||| || |:|:|:| ||| :| ||| ||: |
Db      355 EHFQSIQTLEEQVSGERQRLVETHATRVIALINDQRRAALEGFLAALQGDPPQAERVLN 414
Qy      418 MLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVP 477
      |:|:|:|||:::|:|:|:| |||:| |:| || |:|:| ||||| || |
Db      415 ALRRYLRAEQKEQRHTLRHYQHVAAVDPEKAQQMRQVQVQTHLQVIEERMNQSLGLLDQNP 474
Qy      478 AVAEEIQDEVDELLQKEQNYSDVLANMISEPRISYGN DALMP-SLTETKTTVELLPVNG 536
      :|:|:: :| || || : : || :| | :| |
Db      475 HLAQELRPQIQELL-----LAEHLGPSEL----DASVPGSSSEDK----- 510
Qy      537 EFSLDDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKM 596
      ||| |:::| | :| | : | | : : :
Db      511 ----GSLQP-----PESKDDPPVTLP---KGSTDQESSSSGREKLTPLEQYEQ 551
Qy      597 DAEFRHDSGYEVHH---QKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVML-KKKQ 652
      |: | | : | : : |: |:|:| :| :|:|:|:| |||
Db      552 KVNASAPRGFPFHSSDIQRDELAPSGTGVSREALSGLLIMGAGGSLIVLSLLLLRKKKP 611
Qy      653 YTSIHGVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQ 692
      | :| ||||| | :| ||: | :|:|:| |||||:| |:
Db      612 YGTISHGVVEVDPMLTLEEQQQLRELQRHGYENPTYRFLFEE 651

```

# RESULT 11

JC1404

CDEI-box DNA-binding protein - mouse

C;Species: Mus musculus (house mouse)

C;Date: 30-Sep-1993 #sequence\_revision 30-Sep-1993 #text\_change 16-Feb-1997

C;Accession: JC1404

R;Vidal, F.; Blangy, A.; Rassoulzadegan, M.; Cuzin, F.

Biochem. Biophys. Res. Commun. 189, 1336-1341, 1992

A;Title: A murine sequence-specific DNA binding protein shows extensive local similarities to the amyloid precursor protein.

A;Reference number: JC1404; MUID:93129193; PMID:1482349

A;Accession: JC1404

A;Molecule type: mRNA

A;Residues: 1-511 <VID>

C;Comment: This protein plays an important role in the early development of the mouse.

C;Keywords: DNA binding; transmembrane protein

Query Match 31.3%; Score 1143; DB 2; Length 511;

Best Local Similarity 45.8%; Pred. No. 6e-53;

Matches 253; Conservative 92; Mismatches 128; Indels 80; Gaps 16;



A;Experimental source: strain Bristol N2; clone C42D8  
R;Daigle, I.; Li, C.  
Proc. Natl. Acad. Sci. U.S.A. 90, 12045-12049, 1993  
A;Title: apl-1, a *Caenorhabditis elegans* gene encoding a protein related to the human beta-amyloid protein precursor.  
A;Reference number: A49414; MUID:94089766; PMID:8265668  
A;Accession: A49414  
A;Status: preliminary  
A;Molecule type: mRNA  
A;Residues: 7-686 <DAT>  
A;Cross-references: GB:U00240; NID:g416296; PIDN:AAC46470.1; PID:g416297  
C;Genetics:  
A;Gene: CESP:C42D8.8  
A;Map position: X  
A;Introns: 22/3; 78/3; 121/1; 199/1; 230/1; 274/3; 344/3; 410/2; 471/2; 537/3; 580/3  
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

Query Match 22.4%; Score 817.5; DB 2; Length 686;  
Best Local Similarity 29.1%; Pred. No. 1.1e-35;  
Matches 222; Conservative 110; Mismatches 275; Indels 155; Gaps 22;

```

Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
      :: || : :| | | | | | | | | | | | | | | | | | | | | | | | | |
Db      6 LMIGLLIPILVA-TVYAEGSPAGSKRHEKFIPMVAFSCGYRNQYM-TEEGSWKTDDERYA 63

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
      || | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db     64 TCFSGKLDILKYCRKAYPSMNITNIVEYSHEVSISDWCREEGSPCK-WTHSVRPYHCIDG 122

Qy    121 EFVSDALLVDPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTN-----LHDYGMLLPC 174
      || | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db    123 EFHSEALQVPHDCQFQSHVNSRDQCNDYQHWKDEAGKQCKTKKSKGNKDMIVRSFAVLEPC 182

Qy    175 GIDKFRGVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEV 234
      : | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db    183 ALDMFTGVEFVCCP-----NDQTNKTDVQKTK----- 209

Qy    235 AEVEEEEADDDDEDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTTESVEEVVRVPTTAA 294
      | : | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db    210 ---EEDDDDDDEDDAYEDDYSEESDEKDEE----- 236

Qy    295 STPDAVDKYLETGPDENEHAHFQKAKERLEAKHRERMSQVMREWEEA-----ERQAKNLP 349
      | : | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db    237 -EPSSQDPYFKIANWTNEHDDFKKAEMRMDEKHKRKKVDKVMKEWGDLETRYNEQKAKD-P 294

Qy    350 KADKKAVIQ---HFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITAL- 405
      | : | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db    295 KGAEKFKSQMNARFQKTVSSLEEEHKRMRKEIEAVHEERVQAMLNEKKRDATHDYRQALA 354

Qy    406 -QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYE 464
      | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db    355 THVNKPNKHSVLQSLKAYIRAEKDRMHTLNRYRHLLKADSKEAAAYKPTVIHRLRYIDL 414

Qy    465 RMNQSLSLLYNVP-----AVA--EEIQDEVDELLOKEQNYSDVLANMISEPRISY 513
      | : | | | | | | | | | | | | | | | | | | | | | | | | | | | |

```

```

Db      415 RINGTLAMLRDFPDLEKYVRPIAVTYWKDYRDEVSPDISVE----DSELTPIIHDEFK 470
Qy      514 GN--DALMPSLT----ETKTTVELLPVNGEFSLDDLQPWHSFGADSV PANT---ENEVEP 564
      |  | : |      :      ::||      | : :      : :      |      | : :|
Db      471 NAKLDVKAPTTTAKPVKETDNAKVLPTEASDSEEEADEYYEDEDDEQVKKTPDMKKVKV 530
Qy      565 VDARP-----AADRGLTTRPGSGLTNIKTEE-----ISEVKMDA 598
      || :|      |      |      | : : :|      | : : :|
Db      531 VDIKPKEIKVTIEEEKKAPKLVETSVQTDDDDDDSSSSTSSSEDEDEDKNIKELRVDI 590
Qy      599 E-----FRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMK 649
      |      :|||      ||: |      |      : :      : | | |      :
Db      591 EPIIDEPASFYRHD-----KLIQSPEVERSASSVFQPYVLASAMFITAICIIAFAIT 642
Qy      650 KKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFE 691
      :      | :|||      ||||| : : || ||||| ||| :
Db      643 NARRRRAMRGFIEVD-VYTPEERHVAGMQVNGYENPTYSSFFD 683

```

# RESULT 13

A32758

beta-amyloid-like protein precursor - fruit fly (*Drosophila melanogaster*)

C;Species: *Drosophila melanogaster*

C;Date: 08-Dec-1989 #sequence\_revision 08-Dec-1989 #text\_change 24-Sep-1998

C;Accession: A32758

R;Rosen, D.R.; Martin-Morris, L.; Luo, L.; White, K.

Proc. Natl. Acad. Sci. U.S.A. 86, 2478-2482, 1989

A;Title: A *Drosophila* gene encoding a protein resembling the human beta-amyloid protein precursor.

A;Reference number: A32758; MUID:89184650; PMID:2494667

A;Accession: A32758

A;Status: preliminary

A;Molecule type: mRNA

A;Residues: 1-886 <ROS>

A;Cross-references: GB:J04516; NID:g158371; PID:g158372

C;Genetics:

A;Gene: FlyBase:Appl

A;Cross-references: FlyBase:FBgn0000108

C;Keywords: transmembrane protein

```

Query Match          20.5%; Score 747; DB 2; Length 886;
Best Local Similarity 25.5%; Pred. No. 7.8e-32;
Matches 233; Conservative 127; Mismatches 288; Indels 264; Gaps 29;

```

```

Qy      7 LLLLAAWTARALEVPTDGNAGLLA-----EPQIAMFC--GRLNMHMNV-QNGKWDSDPSG 58
      ||| : |      | :      | | : |      ||||| : |      | : :      : : | : | : |
Db      9 LLLRSLWVVLAI-----GTAQVQAASPRWEPQIAVLCEAGQIYQPQYLSEEGRWVTDLSK 63
Qy      59 T---KTCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRG---RKQCKTHPHFV 112
      ||: |      : | ||: : ||      ||| : ||: :      |      ||: :|      : ||      : :
Db      64 KTTGPTCLRDKMDLLDYCKKAYPNRDITNIVESSHYQKIGGWCRCQALNAACKGSHRWI 123
Qy      113 IPYRCLVGEFVSDALLVDPKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLL 172
      | : ||| | | ||||| : | | |      |      : | :      | | :      : : |||
Db      124 KPFRCCL-GPFQSDALLVPEGCLFDHIHNASRCWPFVWRWNQTGAAACQERGMQMRTFAMLL 182
Qy      173 PCGIDKFRGVEFVCCP-----LAESDNVD---SA 199

```

```

      |||| | |||||
Db      183 PCGISVFGVEFVCCPKHFKTDEIHVKKTDLPVMPAAQINSANDELMNDEDDSDNSNSYK 242
Qy      200 DAEEDDSDVWVGADTDYADGSEDKVVEVAEEEEV-----AEV 237
      || ||| | | | | : : | ||:| ||
Db      243 DANEDDL-----DEDDLMGDDEEDDMVADEAATAGGSPNTGSSGDSNSGSLDDINAAY 296
Qy      238 EE-EEADDDDEDEDGDEVEEEAEPEY-----EEATERT 269
      : || | : | : | | | | : | : | :
Db      297 DSGEEDNYEEDGAGSESEAEVEASWDQSGGAKVVSLKSDSSSPSSAPVAPAPEKAPVKS 356
Qy      270 TSIATTTTTTTSVEEV-----RVPTTAASTPDAVDKYLETPGDENEHAHFQK 318
      | : : | : : | | | | : || | | | | || : :
Db      357 ESVTSTPQLSASAAAFVAANSNGNSGTGAGAPPSTAQPTS---DPYFTHFDPHYEHQSYKV 413
Qy      319 AKERLEAKHRERMSQVMREWEAEERQAKNLPKADKKA-----VIQHFQEKVESLEQEA 371
      : : ||| ||| : : || : | : : : || || : || | : : ||
Db      414 SQKRLEESHREKVTRVMKDWSDLEEKYQDMRLADPKAAQSFQQRMTARFQTSVQALEEEG 473
Qy      372 ANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKYVRAEQKDRQ 431
      | : || | || | : | : | : | || || || | : | : || ||
Db      474 NAEKHQLAAMHQQRVLAHINQRKREAMTCYTQALTEQPPNAHHVEKCLQKLLRALHKDRA 533
Qy      432 HTLKHFEH-VRMVDP---KAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAAVEI----- 483
      | | | : | : | : || | : : | | : ||| : : | | : : |
Db      534 HALAHYRHLLNSGGPGGLEAAAASERPRTLRLIDIDRAVNQSMTMLKRYPELSAKIAQLM 593
Qy      484 -----QDEV----- 487
      : | : :
Db      594 NDYILALRSKDDIPGSSLMSEEAAGILDKYRVEIERKVAEKERLRLAEKQRKEQRAAE 653
Qy      488 -----DELLQKEQNYSDDLANMISE-----PRISYGNDA 519
      : | | : | || : | : : | | | | :
Db      654 REKLREEKLRLAEKKVDDMLKSQVAEQSQPTQSSTQSQAQQQQQEKSLPGKELGPDAAL 713
Qy      520 -----PSLTETKTTVELLPVNGEFSLDDLQPWHSFGADSVPAANTENEVEPVDARPAADRG 574
      | : | || : | | | : : | : | | | | |
Db      714 VTAANPNLETTKS-----EKDLSLTE---YGEATVSTTKVQTVLPTVDDDAVQRA 760
Qy      575 LTTRPGSGLTNIKTEEISEVKMDAEFRHDSGYEVHHQKLVF-----FAEDVGSNK---GA 626
      : : : : : : : : : : | : : | : | : |
Db      761 VEDVAAA-----VAHQEAEPQVQHFMTHDLGHRESSFSLRREFAQHAHAKEGRNV 811
Qy      627 IIGLMVGGVVIATVIVITLVMLKKKQYTSIH-HGVVEVDAVTP-----EERHLSKMQQ 679
      | | : : : : : | : | | | : ||| || || : : ||
Db      812 YFTLSFAGIALMAAVFVGVAWAKWRTSRSPAQGFIEVDQNVTTTHPIVREEKIVPNMQI 871
Qy      680 NGYENPTYKFFE 691
      ||||| ||| : ||
Db      872 NGYENPTYKYFE 883

```

RESULT 14

S38344

CDEI-binding protein - mouse (fragment)

C;Species: Mus musculus (house mouse)

C;Date: 19-May-1994 #sequence\_revision 26-May-1995 #text\_change 03-May-1996



C;Accession: S38344  
 R;Hanes, J.; von der Kammer, H.; Kristjansson, G.I.; Scheit, K.H.  
 Biochim. Biophys. Acta 1216, 154-156, 1993  
 A;Title: The complete cDNA coding sequence for the mouse CDEI binding protein.  
 A;Reference number: S38344; MUID:94032480; PMID:8218408  
 A;Accession: S38344  
 A;Status: preliminary  
 A;Molecule type: mRNA  
 A;Residues: 1-246 <HAN>  
 A;Cross-references: EMBL:Z22592  
 C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type  
 proteinase inhibitor homology

Query Match 19.3%; Score 706; DB 2; Length 246;  
 Best Local Similarity 51.5%; Pred. No. 2.2e-30;  
 Matches 136; Conservative 35; Mismatches 51; Indels 42; Gaps 7;

```

Qy      5 LALLLLAAWTARALEV-----PTDGNAG---LLAEPQIAMFCGRLNMHMNVQNGKWSDP 56
      | :|||  || | :          |||  :||| ||| ||:||||:|:| |||: ||
Db     15 LLVLLLLGLTAPAAALAGYIEALAANAGTGFVAEAPQIAMLCGKLNMHVNIQTGWEPDP 74

Qy     57 SGTKTCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYR 116
      :|||:|: ||| :||| |||:||||| |||:||||| | :||:| :|||: | |||::
Db     75 TGTKSCLGTKEEVLQYCQEIYPELQITNVMEANQPVNIDSWCRRDKRQCKS--HIVIPFK 132

Qy    117 CLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLP CGI 176
      ||||| |||| | :| ||||: ||| | |||: || | : | : ||||| :
Db    133 CLVGEFVSDVLLVPDNCQFFHQERMEVCEKHQRWHTLVKEACLTEGLTLYSGMLLP CGV 192

Qy    177 DKFRGVEFVCCPLAEESDNVDSADAEEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAE 236
      |:| | |:|||  :: |||  | : |||
Db    193 DQFHGTEYVCCP---QTKTVDS-----DSTMSKEEEEE--- 222

Qy    237 VEEEEADDDDED-DEDGDEVEEEAE 259
      ||:| |:|| | | | ||:
Db    223 -EEDEEDEEEDYDLKSEFPTEAD 245
  
```

# RESULT 15

PQ0438

Alzheimer's disease amyloid A4 protein precursor - rabbit (fragment)

C;Species: Oryctolagus cuniculus (domestic rabbit)

C;Date: 30-Sep-1993 #sequence\_revision 19-Oct-1995 #text\_change 19-Oct-1995

C;Accession: PQ0438; C60045

R;Davidson, J.S.; West, R.L.; Kotikalapudi, P.; Maroun, L.E.

Biochem. Biophys. Res. Commun. 188, 905-911, 1992

A;Title: Sequence and methylation in the beta/A4 region of the rabbit amyloid precursor protein gene.

A;Reference number: PQ0438; MUID:93075180; PMID:1445331

A;Accession: PQ0438

A;Molecule type: DNA

A;Residues: 1-82 <DAV>

A;Cross-references: GB:M83558; GB:M83657

R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.

Brain Res. Mol. Brain Res. 10, 299-305, 1991

A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide in dog, polar bear and five other mammals by cross-species polymerase chain reaction analysis.

A;Reference number: A60045; MUID:92017079; PMID:1656157

A;Accession: C60045

A;Molecule type: mRNA

A;Residues: 12-68 <JOH>

A;Cross-references: EMBL:X56129

C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

C;Keywords: alternative splicing; Alzheimer's disease; amyloid; Down's syndrome

Query Match 11.3%; Score 411; DB 2; Length 82;

Best Local Similarity 100.0%; Pred. No. 1.8e-15;

Matches 82; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 581 SGLTNIKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATV 640

|||||

Db 1 SGLTNIKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATV 60

Qy 641 IVITLVMLKKKQYTSIHGGVVE 662

|||||

Db 61 IVITLVMLKKKQYTSIHGGVVE 82

Search completed: July 26, 2004, 12:47:25

Job time : 16.6667 secs

GenCore version 5.1.6  
Copyright (c) 1993 - 2004 Compugen Ltd.

OM protein - protein search, using sw model

Run on: July 26, 2004, 12:46:43 ; Search time 44.3333 Seconds  
(without alignments)  
4923.349 Million cell updates/sec

Title: US-09-806-194A-16  
Perfect score: 3651  
Sequence: 1 MLPGLALLLLAAWTARALEV.....QQNGYENPTYKFFEQMQNKK 697

Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5

Searched: 1288442 seqs, 313154207 residues

Total number of hits satisfying chosen parameters: 1288442

Minimum DB seq length: 0  
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

Database : Published\_Applications\_AA:\*  
1: /cgn2\_6/ptodata/1/pubpaa/US07\_PUBCOMB.pep:\*  
2: /cgn2\_6/ptodata/1/pubpaa/PCT\_NEW\_PUB.pep:\*  
3: /cgn2\_6/ptodata/1/pubpaa/US06\_NEW\_PUB.pep:\*  
4: /cgn2\_6/ptodata/1/pubpaa/US06\_PUBCOMB.pep:\*  
5: /cgn2\_6/ptodata/1/pubpaa/US07\_NEW\_PUB.pep:\*  
6: /cgn2\_6/ptodata/1/pubpaa/PCTUS\_PUBCOMB.pep:\*  
7: /cgn2\_6/ptodata/1/pubpaa/US08\_NEW\_PUB.pep:\*  
8: /cgn2\_6/ptodata/1/pubpaa/US08\_PUBCOMB.pep:\*  
9: /cgn2\_6/ptodata/1/pubpaa/US09A\_PUBCOMB.pep:\*  
10: /cgn2\_6/ptodata/1/pubpaa/US09B\_PUBCOMB.pep:\*  
11: /cgn2\_6/ptodata/1/pubpaa/US09C\_PUBCOMB.pep:\*  
12: /cgn2\_6/ptodata/1/pubpaa/US09\_NEW\_PUB.pep:\*  
13: /cgn2\_6/ptodata/1/pubpaa/US10A\_PUBCOMB.pep:\*  
14: /cgn2\_6/ptodata/1/pubpaa/US10B\_PUBCOMB.pep:\*  
15: /cgn2\_6/ptodata/1/pubpaa/US10C\_PUBCOMB.pep:\*  
16: /cgn2\_6/ptodata/1/pubpaa/US10\_NEW\_PUB.pep:\*  
17: /cgn2\_6/ptodata/1/pubpaa/US60\_NEW\_PUB.pep:\*  
18: /cgn2\_6/ptodata/1/pubpaa/US60\_PUBCOMB.pep:\*

Pred. No. is the number of results predicted by chance to have a  
score greater than or equal to the score of the result being printed,  
and is derived by analysis of the total score distribution.

SUMMARIES

Result	%	Query				
No.	Score	Match Length DB	ID			Description

1	3651	100.0	697	9	US-09-794-927-16	Sequence 16, Appl
2	3651	100.0	697	9	US-09-795-847-16	Sequence 16, Appl
3	3651	100.0	697	9	US-09-794-743-16	Sequence 16, Appl
4	3651	100.0	697	9	US-09-794-748-16	Sequence 16, Appl
5	3651	100.0	697	9	US-09-794-925-16	Sequence 16, Appl
6	3651	100.0	697	9	US-09-681-442-16	Sequence 16, Appl
7	3651	100.0	697	10	US-09-869-414-16	Sequence 16, Appl
8	3651	100.0	697	10	US-09-548-366-16	Sequence 16, Appl
9	3651	100.0	697	12	US-10-652-927-16	Sequence 16, Appl
10	3651	100.0	697	12	US-10-652-830-16	Sequence 16, Appl
11	3646	99.9	697	9	US-09-794-927-20	Sequence 20, Appl
12	3646	99.9	697	9	US-09-795-847-20	Sequence 20, Appl
13	3646	99.9	697	9	US-09-794-743-20	Sequence 20, Appl
14	3646	99.9	697	9	US-09-794-748-20	Sequence 20, Appl
15	3646	99.9	697	9	US-09-794-925-20	Sequence 20, Appl
16	3646	99.9	697	9	US-09-681-442-20	Sequence 20, Appl
17	3646	99.9	697	10	US-09-869-414-20	Sequence 20, Appl
18	3646	99.9	697	10	US-09-548-366-20	Sequence 20, Appl
19	3646	99.9	697	12	US-10-652-927-20	Sequence 20, Appl
20	3646	99.9	697	12	US-10-652-830-20	Sequence 20, Appl
21	3643	99.8	697	9	US-09-794-927-18	Sequence 18, Appl
22	3643	99.8	697	9	US-09-795-847-18	Sequence 18, Appl
23	3643	99.8	697	9	US-09-794-743-18	Sequence 18, Appl
24	3643	99.8	697	9	US-09-794-748-18	Sequence 18, Appl
25	3643	99.8	697	9	US-09-794-925-18	Sequence 18, Appl
26	3643	99.8	697	9	US-09-681-442-18	Sequence 18, Appl
27	3643	99.8	697	10	US-09-869-414-18	Sequence 18, Appl
28	3643	99.8	697	10	US-09-548-366-18	Sequence 18, Appl
29	3643	99.8	697	12	US-10-652-927-18	Sequence 18, Appl
30	3643	99.8	697	12	US-10-652-830-18	Sequence 18, Appl
31	3641	99.7	695	9	US-09-794-927-10	Sequence 10, Appl
32	3641	99.7	695	9	US-09-795-847-10	Sequence 10, Appl
33	3641	99.7	695	9	US-09-794-743-10	Sequence 10, Appl
34	3641	99.7	695	9	US-09-794-748-10	Sequence 10, Appl
35	3641	99.7	695	9	US-09-794-925-10	Sequence 10, Appl
36	3641	99.7	695	9	US-09-681-442-10	Sequence 10, Appl
37	3641	99.7	695	9	US-09-149-718-2	Sequence 2, Appli
38	3641	99.7	695	10	US-09-869-414-10	Sequence 10, Appl
39	3641	99.7	695	10	US-09-548-366-10	Sequence 10, Appl
40	3641	99.7	695	10	US-09-998-491-1	Sequence 1, Appli
41	3641	99.7	695	12	US-10-652-927-10	Sequence 10, Appl
42	3641	99.7	695	12	US-10-652-830-10	Sequence 10, Appl
43	3641	99.7	695	14	US-10-169-580-3	Sequence 3, Appli
44	3641	99.7	695	14	US-10-357-935-1	Sequence 1, Appli
45	3641	99.7	695	15	US-10-427-208-45	Sequence 45, Appl

#### ALIGNMENTS

RESULT 1  
 US-09-794-927-16  
 ; Sequence 16, Application US/09794927  
 ; Patent No. US20010016324A1  
 ; GENERAL INFORMATION:  
 ; APPLICANT: Gurney, Mark E.

```

; APPLICANT: Bienkowski, Michael J.
; APPLICANT: Heinrikson, Robert L.
; APPLICANT: Parodi, Luis A.
; APPLICANT: Yan, Riqiang
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,
AND
; TITLE OF INVENTION: USES
; TITLE OF INVENTION: THEREFOR
; FILE REFERENCE: 28341/6280FG
; CURRENT APPLICATION NUMBER: US/09/794,927
; CURRENT FILING DATE: 2001-02-27
; PRIOR APPLICATION NUMBER: 09/416,901
; PRIOR FILING DATE: 1999-10-13
; PRIOR APPLICATION NUMBER: 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 16
; LENGTH: 697
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-794-927-16

```

```

Query Match          100.0%; Score 3651; DB 9; Length 697;
Best Local Similarity 100.0%; Pred. No. 1.3e-223;
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```

```

Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60
|
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
|
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
|
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
|
Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEEPYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV 300
|
Db    241 EADDDDEDDEDGDEVEEEAEEPYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360
|
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360

```

Qy 361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420  
 |||  
 Db 361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480  
 |||  
 Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480

Qy 481 EEIQDEVDELLOKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540  
 |||  
 Db 481 EEIQDEVDELLOKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540

Qy 541 DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600  
 |||  
 Db 541 DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMMLKKQYTSIHHGV 660  
 |||  
 Db 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMMLKKQYTSIHHGV 660

Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697  
 |||  
 Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697

RESULT 2

US-09-795-847-16

; Sequence 16, Application US/09795847

; Patent No. US20010018208A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,

AND

; TITLE OF INVENTION: USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280DE

; CURRENT APPLICATION NUMBER: US/09/795,847

; CURRENT FILING DATE: 2001-02-28

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn Ver. 2.0

; SEQ ID NO 16

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens  
US-09-795-847-16

Query Match 100.0%; Score 3651; DB 9; Length 697;  
Best Local Similarity 100.0%; Pred. No. 1.3e-223;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60
      |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
      |||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
      |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
      |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
      |||
Db    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360
      |||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
      |||
Db    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPVA 480
      |||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPVA 480

Qy    481 EEIQDEVDELLQKEQNYSDDLANMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540
      |||
Db    481 EEIQDEVDELLQKEQNYSDDLANMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600
      |||
Db    541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy    601 RHDSGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITLVMLKKKQYTSIHG 660
      |||
Db    601 RHDSGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITLVMLKKKQYTSIHG 660

Qy    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697
      |||
Db    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697
```

RESULT 3

US-09-794-743-16  
; Sequence 16, Application US/09794743  
; Patent No. US20010021391A1  
; GENERAL INFORMATION:  
; APPLICANT: Gurney, Mark E.  
; APPLICANT: Bienkowski, Michael J.  
; APPLICANT: Heinrikson, Robert L.  
; APPLICANT: Parodi, Luis A.  
; APPLICANT: Yan, Riqiang  
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,  
AND  
; TITLE OF INVENTION: USES  
; TITLE OF INVENTION: THEREFOR  
; FILE REFERENCE: 28341/6280BC  
; CURRENT APPLICATION NUMBER: US/09/794,743  
; CURRENT FILING DATE: 2001-02-27  
; PRIOR APPLICATION NUMBER: 09/416,901  
; PRIOR FILING DATE: 1999-10-13  
; PRIOR APPLICATION NUMBER: 60/155,493  
; PRIOR FILING DATE: 1999-09-23  
; PRIOR APPLICATION NUMBER: 09/404,133  
; PRIOR FILING DATE: 1999-09-23  
; PRIOR APPLICATION NUMBER: PCT/US99/20881  
; PRIOR FILING DATE: 1999-09-23  
; PRIOR APPLICATION NUMBER: 60/101,594  
; PRIOR FILING DATE: 1998-09-24  
; NUMBER OF SEQ ID NOS: 73  
; SOFTWARE: PatentIn Ver. 2.0  
; SEQ ID NO 16  
; LENGTH: 697  
; TYPE: PRT  
; ORGANISM: Homo sapiens  
US-09-794-743-16

Query Match 100.0%; Score 3651; DB 9; Length 697;  
Best Local Similarity 100.0%; Pred. No. 1.3e-223;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300



Qy 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360  
 |||  
 Db 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360

Qy 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420  
 |||  
 Db 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480  
 |||  
 Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480

Qy 481 EEIQDEVDPELLQKEQNYSDDLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL 540  
 |||  
 Db 481 EEIQDEVDPELLQKEQNYSDDLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL 540

Qy 541 DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600  
 |||  
 Db 541 DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy 601 RHDSGYEVHHQKLFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660  
 |||  
 Db 601 RHDSGYEVHHQKLFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660

Qy 661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMQNKK 697  
 |||  
 Db 661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMQNKK 697

RESULT 4

US-09-794-748-16

; Sequence 16, Application US/09794748

; Patent No. US20020037315A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,  
 AND

; TITLE OF INVENTION: USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280JL

; CURRENT APPLICATION NUMBER: US/09/794,748

; CURRENT FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73  
; SOFTWARE: PatentIn Ver. 2.0  
; SEQ ID NO 16  
; LENGTH: 697  
; TYPE: PRT  
; ORGANISM: Homo sapiens  
US-09-794-748-16

Query Match 100.0%; Score 3651; DB 9; Length 697;  
Best Local Similarity 100.0%; Pred. No. 1.3e-223;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEEPYYEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV 300
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    241 EADDDDEDDEDGDEVEEEAEEPYYEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRRLALENYITALQAVPPRPRHVFNMLK 420
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy    481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL 540
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    541 DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMMLKKKQYTSIHHGV 660
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMMLKKKQYTSIHHGV 660

Qy    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697
```

|||||  
Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697

RESULT 5

US-09-794-925-16

; Sequence 16, Application US/09794925

; Patent No. US20020064819A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,  
AND USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280HI

; CURRENT APPLICATION NUMBER: US/09/794,925

; CURRENT FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn Ver. 2.0

; SEQ ID NO 16

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-794-925-16

Query Match 100.0%; Score 3651; DB 9; Length 697;

Best Local Similarity 100.0%; Pred. No. 1.3e-223;

Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60  
|  
Db 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60  
  
Qy 61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120  
|  
Db 61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120  
  
Qy 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180  
|  
Db 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180  
  
Qy 181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240  
|  
Db 181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy 241 EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300  
 |||  
 Db 241 EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360  
 |||  
 Db 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360

Qy 361 QEKVESLEQEAAERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420  
 |||  
 Db 361 QEKVESLEQEAAERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy 421 KYVRAEQKDRQHTLKHFEHVRMVDPKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480  
 |||  
 Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNLMPSLTETKTTVELLPVNGEFSL 540  
 |||  
 Db 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNLMPSLTETKTTVELLPVNGEFSL 540

Qy 541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600  
 |||  
 Db 541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy 601 RHDSGYEVHHQKLFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660  
 |||  
 Db 601 RHDSGYEVHHQKLFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660

Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697  
 |||  
 Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697

# RESULT 6

US-09-681-442-16

; Sequence 16, Application US/09681442

; Patent No. US20020081634A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR, AND USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280FG

; CURRENT APPLICATION NUMBER: US/09/681,442

; CURRENT FILING DATE: 2001-04-05

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23  
; PRIOR APPLICATION NUMBER: 60/101,594  
; PRIOR FILING DATE: 1998-09-24  
; NUMBER OF SEQ ID NOS: 73  
; SOFTWARE: PatentIn Ver. 2.0  
; SEQ ID NO 16  
; LENGTH: 697  
; TYPE: PRT  
; ORGANISM: Homo sapiens  
US-09-681-442-16

Query Match 100.0%; Score 3651; DB 9; Length 697;  
Best Local Similarity 100.0%; Pred. No. 1.3e-223;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDEDGDEVEEEAEEPYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDEDGDEVEEEAEEPYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLFFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660



Qy 241 EADDDDEDEDGDEVEEEAEFPYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV 300  
 |||  
 Db 241 EADDDDEDEDGDEVEEEAEFPYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360  
 |||  
 Db 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360

Qy 361 QEKVESLEQEAAANERQQVLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420  
 |||  
 Db 361 QEKVESLEQEAAANERQQVLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480  
 |||  
 Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480

Qy 481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL 540  
 |||  
 Db 481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL 540

Qy 541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600  
 |||  
 Db 541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy 601 RHDSGYEVHHQKLVFFAEDVGSNGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV 660  
 |||  
 Db 601 RHDSGYEVHHQKLVFFAEDVGSNGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV 660

Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697  
 |||  
 Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697

RESULT 8

US-09-548-366-16

; Sequence 16, Application US/09548366

; Publication No. US20030104365A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,  
 AND

; TITLE OF INVENTION: USES THEREFOR

; FILE REFERENCE: 28341/6280A

; CURRENT APPLICATION NUMBER: US/09/548,366

; CURRENT FILING DATE: 2000-04-12

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 65  
; SOFTWARE: PatentIn Ver. 2.0  
; SEQ ID NO 16  
; LENGTH: 697  
; TYPE: PRT  
; ORGANISM: Homo sapiens  
US-09-548-366-16

Query Match 100.0%; Score 3651; DB 10; Length 697;  
Best Local Similarity 100.0%; Pred. No. 1.3e-223;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
      |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
      |||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLP CGIDKFR 180
      |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLP CGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240
      |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV 300
      |||
Db    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360
      |||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAANERQQVLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
      |||
Db    361 QEKVESLEQEAANERQQVLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA 480
      |||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA 480

Qy    481 EEIQDEVDELLQKEQNYSDDLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL 540
      |||
Db    481 EEIQDEVDELLQKEQNYSDDLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600
      |||
Db    541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy    601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660
      |||
Db    601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660

Qy    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697
```



|||||  
Db 661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMQNKK 697

RESULT 9

US-10-652-927-16

; Sequence 16, Application US/10652927

; Publication No. US20040043408A1

; GENERAL INFORMATION:

; APPLICANT: Gurney et al.

; TITLE OF INVENTION: Alzheimer's Disease Secretase, APP Substrates Therefor  
and Uses

; TITLE OF INVENTION: Therefor

; FILE REFERENCE: 29915/6280N3

; CURRENT APPLICATION NUMBER: US/10/652,927

; CURRENT FILING DATE: 2003-08-29

; PRIOR APPLICATION NUMBER: 09/794,925

; PRIOR FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 74

; SOFTWARE: PatentIn Ver. 2.0

; SEQ ID NO 16

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-10-652-927-16

Query Match 100.0%; Score 3651; DB 12; Length 697;

Best Local Similarity 100.0%; Pred. No. 1.3e-223;

Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
      |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
      |||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMMLPCGIDKFR 180
      |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMMLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEEDSDVWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
      |||
Db    181 GVEFVCCPLAEESDNVDSADAEEEDSDVWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDGDEVEEEAEOPYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
```

Db	241	EADDDDEDDGDEVEEEAEEPYYEATERTTSIATTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLYNVPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLYNVPAVA	480
Qy	481	EEIQDEVDELLOKEQNYSDDLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLOKEQNYSDDLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697

RESULT 10

US-10-652-830-16

; Sequence 16, Application US/10652830

; Publication No. US20040048303A1

; GENERAL INFORMATION:

; APPLICANT: Gurney et al.

; TITLE OF INVENTION: Alzheimer's Disease Secretase, APP Substrates Therefor and Uses

; TITLE OF INVENTION: Therefor

; FILE REFERENCE: 29915/6280N1

; CURRENT APPLICATION NUMBER: US/10/652,830

; CURRENT FILING DATE: 2003-08-29

; PRIOR APPLICATION NUMBER: 09/794,925

; PRIOR FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 74

; SOFTWARE: PatentIn Ver. 2.0  
; SEQ ID NO 16  
; LENGTH: 697  
; TYPE: PRT  
; ORGANISM: Homo sapiens  
US-10-652-830-16

Query Match 100.0%; Score 3651; DB 12; Length 697;  
Best Local Similarity 100.0%; Pred. No. 1.3e-223;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLIAEPQIAMFCGRLNMHMNVQNGKWDSDPSGK 60
        |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLIAEPQIAMFCGRLNMHMNVQNGKWDSDPSGK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
        |||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240
        |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240

Qy    241 EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
        |||
Db    241 EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
        |||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
        |||
Db    361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480
        |||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480

Qy    481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540
        |||
Db    481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600
        |||
Db    541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy    601 RHDSGYEVHHQKLFFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660
        |||
Db    601 RHDSGYEVHHQKLFFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660

Qy    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697
        |||
```

RESULT 11

US-09-794-927-20

; Sequence 20, Application US/09794927

; Patent No. US20010016324A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,

AND

; TITLE OF INVENTION: USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280FG

; CURRENT APPLICATION NUMBER: US/09/794,927

; CURRENT FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: .60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn Ver. 2.0

; SEQ ID NO 20

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-794-927-20

Query Match 99.9%; Score 3646; DB 9; Length 697;

Best Local Similarity 99.9%; Pred. No. 2.7e-223;

Matches 696; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240

Qy 241 EADDDDEDDGDEVEEEAEEPYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300  
 |||  
 Db 241 EADDDDEDDGDEVEEEAEEPYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360  
 |||  
 Db 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360

Qy 361 QEKVESLEQEAAANERQQVLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420  
 |||  
 Db 361 QEKVESLEQEAAANERQQVLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPVA 480  
 |||  
 Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPVA 480

Qy 481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYNDALMPSLTETKTTVELLPVNGEFS 540  
 |||  
 Db 481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYNDALMPSLTETKTTVELLPVNGEFS 540

Qy 541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600  
 |||  
 Db 541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV 660  
 |||  
 Db 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHGGV 660

Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697  
 |||  
 Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697

RESULT 12

US-09-795-847-20

; Sequence 20, Application US/09795847

; Patent No. US20010018208A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,  
 AND

; TITLE OF INVENTION: USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280DE

; CURRENT APPLICATION NUMBER: US/09/795,847

; CURRENT FILING DATE: 2001-02-28

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881  
; PRIOR FILING DATE: 1999-09-23  
; PRIOR APPLICATION NUMBER: 60/101,594  
; PRIOR FILING DATE: 1998-09-24  
; NUMBER OF SEQ ID NOS: 73  
; SOFTWARE: PatentIn Ver. 2.0  
; SEQ ID NO 20  
; LENGTH: 697  
; TYPE: PRT  
; ORGANISM: Homo sapiens  
US-09-795-847-20

Query Match 99.9%; Score 3646; DB 9; Length 697;  
Best Local Similarity 99.9%; Pred. No. 2.7e-223;  
Matches 696; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQIVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQIVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660

Db 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMKKKQYTSIHGGV 660  
 Qy 661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMONKK 697  
 Db 661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMONKK 697

RESULT 13

US-09-794-743-20

; Sequence 20, Application US/09794743

; Patent No. US20010021391A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,  
AND

; TITLE OF INVENTION: USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280BC

; CURRENT APPLICATION NUMBER: US/09/794,743

; CURRENT FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

```
; SOFTWARE: PatentIn Ver. 2.0
```

; SEQ ID NO 20

; LENGTH: 697

```
; TYPE: PRT
```

; ORGANISM: Homo sapiens

US-09-794-743-20

Query Match 99.9%; Score 3646; DB 9; Length 697;

Best Local Similarity 99.9%; Pred. No. 2.7e-223;

Matches 696; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

QY 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRNMHMNVQNGKWDSDPSTGK 60

Db 1 MLPLGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRNLNMHNMNVQNGKWDSDPSGTK 60

QY 61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Db 61 TCIDTKEGILQYQCQEVYPELQITNVVEANQPVTIONWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

\_\_\_\_\_

Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDEDGDEVEEEAEOPYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDEDGDEVEEEAEOPYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDDLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDDLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLVEFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGCV	660
Db	601	RHDSGYEVHHQKLVEFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGCV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK	697

RESULT 14

US-09-794-748-20

; Sequence 20, Application US/09794748

; Patent No. US20020037315A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,

AND

; TITLE OF INVENTION: USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280JL

; CURRENT APPLICATION NUMBER: US/09/794,748

; CURRENT FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901



; PRIOR FILING DATE: 1999-10-13  
; PRIOR APPLICATION NUMBER: 60/155,493  
; PRIOR FILING DATE: 1999-09-23  
; PRIOR APPLICATION NUMBER: 09/404,133  
; PRIOR FILING DATE: 1999-09-23  
; PRIOR APPLICATION NUMBER: PCT/US99/20881  
; PRIOR FILING DATE: 1999-09-23  
; PRIOR APPLICATION NUMBER: 60/101,594  
; PRIOR FILING DATE: 1998-09-24  
; NUMBER OF SEQ ID NOS: 73  
; SOFTWARE: PatentIn Ver. 2.0  
; SEQ ID NO 20  
; LENGTH: 697  
; TYPE: PRT  
; ORGANISM: Homo sapiens  
US-09-794-748-20

Query Match 99.9%; Score 3646; DB 9; Length 697;  
Best Local Similarity 99.9%; Pred. No. 2.7e-223;  
Matches 696; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDGEDGVEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDGEDGVEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQVLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQVLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDDLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDDLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540

Qy 541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600  
 |||  
 Db 541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV 660  
 |||  
 Db 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHGGV 660

Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697  
 |||  
 Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697

RESULT 15

US-09-794-925-20

; Sequence 20, Application US/09794925

; Patent No. US20020064819A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,  
 AND USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280HI

; CURRENT APPLICATION NUMBER: US/09/794,925

; CURRENT FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn Ver. 2.0

; SEQ ID NO 20

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-794-925-20

Query Match 99.9%; Score 3646; DB 9; Length 697;

Best Local Similarity 99.9%; Pred. No. 2.7e-223;

Matches 696; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

Qy 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60  
 |||

Db 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy 61 TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120  
 |||

Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMP\$LTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMP\$LTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697

Search completed: July 26, 2004, 13:00:42  
Job time : 46.3333 secs

OM protein - protein search, using sw model

Run on: July 26, 2004, 12:39:53 ; Search time 35.3333 Seconds  
(without alignments)  
6224.043 Million cell updates/sec

Title: US-09-806-194A-16  
Perfect score: 3651  
Sequence: 1 MLPGLALLLLAAWTARALEV.....QQNGYENPTYKFFEQMQNKK 697

Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5

Searched: 1017041 seqs, 315518202 residues

Total number of hits satisfying chosen parameters: 1017041

Minimum DB seq length: 0  
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

Database : SPTREMBL\_25:\*  
1: sp\_archaea:\*  
2: sp\_bacteria:\*  
3: sp\_fungi:\*  
4: sp\_human:\*  
5: sp\_invertebrate:\*  
6: sp\_mammal:\*  
7: sp\_mhc:\*  
8: sp\_organelle:\*  
9: sp\_phage:\*  
10: sp\_plant:\*  
11: sp\_rodent:\*  
12: sp\_virus:\*  
13: sp\_vertebrate:\*  
14: sp\_unclassified:\*  
15: sp\_rvirus:\*  
16: sp\_bacteriap:\*  
17: sp\_archeap:\*

Pred. No. is the number of results predicted by chance to have a  
score greater than or equal to the score of the result being printed,  
and is derived by analysis of the total score distribution.

#### SUMMARIES

		%			
Result		Query			
No.	Score	Match	Length	ID	Description
-----					

1	3428	93.9	695	13	Q9DGJ8	Q9dgj8	gallus gall
2	3387	92.8	751	13	Q9DGJ7	Q9dgj7	gallus gall
3	3214	88.0	693	13	Q98SG0	Q98sg0	xenopus lae
4	3190	87.4	695	13	Q98SF9	Q98sf9	xenopus lae
5	3188	87.3	695	13	Q7ZXQ0	Q7zxq0	xenopus lae
6	3103	85.0	747	13	Q91963	Q91963	xenopus. ap
7	2964.5	81.2	699	13	O57394	O57394	narke japon
8	2767.5	75.8	569	13	Q9PVL1	Q9pvl1	gallus gall
9	2613	71.6	534	13	O93296	O93296	gallus gall
10	2567	70.3	678	13	Q7ZZT1	Q7zzt1	brachydanio
11	2529	69.3	738	13	Q90W28	Q90w28	brachydanio
12	2487.5	68.1	694	13	Q8UUR9	Q8uur9	brachydanio
13	2339	64.1	612	13	Q9I9E7	Q9i9e7	brachydanio
14	1928	52.8	384	11	Q8BPC7	Q8bpc7	mus musculu
15	1762	48.3	695	4	Q13861	Q13861	homo sapien
16	1749.5	47.9	669	4	Q14662	Q14662	homo sapien
17	1744	47.8	707	11	Q80US7	Q80us7	mus musculu
18	1740	47.7	695	11	Q64348	Q64348	mus musculu
19	1731	47.4	715	11	Q7TT34	Q7tt34	mus musculu
20	1708	46.8	763	11	Q61482	Q61482	mus musculu
21	1704	46.7	751	11	Q60709	Q60709	mus musculu
22	1655	45.3	472	13	Q8UUS0	Q8uus0	brachydanio
23	1350.5	37.0	357	13	Q8UUI8	Q8uui8	brachydanio
24	1301.5	35.6	522	4	Q9BT36	Q9bt36	homo sapien
25	1090	29.9	218	11	Q8BPV5	Q8bpv5	mus musculu
26	1048.5	28.7	523	4	Q14594	Q14594	homo sapien
27	795	21.8	357	13	Q7ZZT2	Q7zzt2	brachydanio
28	771	21.1	239	13	Q8UUI7	Q8uui7	brachydanio
29	577	15.8	113	13	Q8JH58	Q8jh58	chelydra se
30	561	15.4	182	11	Q9CYS4	Q9cys4	mus musculu
31	478	13.1	97	6	Q28673	Q28673	oryctolagus
32	435.5	11.9	140	13	Q800X9	Q800x9	chelydra se
33	393.5	10.8	82	4	Q16019	Q16019	homo sapien
34	389.5	10.7	82	4	Q16014	Q16014	homo sapien
35	387.5	10.6	82	4	Q16020	Q16020	homo sapien
36	376	10.3	79	11	O35463	O35463	cricketulus
37	358.5	9.8	160	11	Q9QZ78	Q9qz78	cavia sp. p
38	335	9.2	208	11	Q8R0R7	Q8r0r7	mus musculu
39	239	6.5	49	6	O97917	O97917	bos taurus
40	196.5	5.4	727	5	Q95TG7	Q95tg7	drosophila
41	196.5	5.4	5303	5	Q9V628	Q9v628	drosophila
42	193	5.3	785	5	Q9GQ82	Q9gq82	drosophila
43	192.5	5.3	556	5	Q95S93	Q95s93	drosophila
44	192.5	5.3	1110	13	Q91255	Q91255	petromyzon
45	191.5	5.2	556	5	Q9V7I9	Q9v7i9	drosophila

#### ALIGNMENTS

##### RESULT 1

Q9DGJ8

ID	Q9DGJ8	PRELIMINARY;	PRT;	695 AA.
AC	Q9DGJ8;			
DT	01-MAR-2001 (TrEMBLrel. 16, Created)			
DT	01-MAR-2001 (TrEMBLrel. 16, Last sequence update)			
DT	01-JUN-2003 (TrEMBLrel. 24, Last annotation update)			



Qy 419 LKKYVRAEQKDRQHTLKHFHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPA 478  
 |||  
 Db 419 LKKYVRAEQKDRQHTLKHFHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLFLYNVPA 478  
 Qy 479 VAEELIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEF 538  
 |||:|  
 Db 479 VAEELIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVDGEF 538  
 Qy 539 SLDDLQPWHSFGADSVDPANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDA 598  
 |||:|:|  
 Db 539 SLDDLQPWHPFGVDSVPANTENEVEPVDARPAADRGLTTRPGSGLTNVKTEEVESEVKMDA 598  
 Qy 599 EFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMKKKQYTSIHH 658  
 |||  
 Db 599 EFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMKKKQYTSIHH 658  
 Qy 659 GVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695  
 |||  
 Db 659 GVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695

RESULT 2

Q9DGJ7

ID Q9DGJ7 PRELIMINARY; PRT; 751 AA.  
 AC Q9DGJ7;  
 DT 01-MAR-2001 (TrEMBLrel. 16, Created)  
 DT 01-MAR-2001 (TrEMBLrel. 16, Last sequence update)  
 DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)  
 DE Beta-amyloid precursor protein 751 isoform.  
 OS Gallus gallus (Chicken).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;  
 OC Gallus.  
 OX NCBI\_TaxID=9031;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RA Sarasa M., Rodolosse A., Sorribas V.;  
 RT "Cloning of full-length chicken beta-amyloid precursor protein  
 RT isoforms."  
 RL Submitted (JUL-2000) to the EMBL/GenBank/DDBJ databases.  
 DR EMBL; AF289219; AAG00594.1; -.  
 DR HSSP; P05067; 1BA4.  
 DR GO; GO:0016020; C:membrane; IEA.  
 DR GO; GO:0004867; F:serine protease inhibitor activity; IEA.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR InterPro; IPR002223; Kunitz\_BPTI.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR Pfam; PF00014; Kunitz\_BPTI; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR PRINTS; PR00759; BASICPTASE.  
 DR ProDom; PD000222; Kunitz\_BPTI; 1.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR SMART; SM00131; KU; 1.

DR PROSITE; PS00319; A4\_EXTRA; 1.  
DR PROSITE; PS00320; A4\_INTRA; 1.  
DR PROSITE; PS00280; BPTI\_KUNITZ\_1; 1.  
DR PROSITE; PS00279; BPTI\_KUNITZ\_2; 1.  
KW Protease inhibitor; Serine protease inhibitor.  
SQ SEQUENCE 751 AA; 84705 MW; E78E9413A8033D84 CRC64;

Query Match 92.8%; Score 3387; DB 13; Length 751;  
Best Local Similarity 86.9%; Pred. No. 2.1e-195;  
Matches 654; Conservative 18; Mismatches 21; Indels 60; Gaps 4;

```
Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
      ||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      1 MLPHLALLLLAAGAAARALEVPADGNAGLLAEPQIAMFCGKLNMHMNVQNGKWESDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120
      ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGWKQCNGHPHIVVPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
      ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    121 EFVSDALLVPDKCKLLHQERMDVCETHLHWHTVAKESCSEKSMNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDDSDVWWGGADTDYADGSEDKVVE--VAEEEEVAEVE 238
      ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    181 GVEFVCCPLAEESDNLDSADAEDDDSDVWWGGADADYADGSDDKVVEEQPEEDEELTVVE 240

Qy    239 EEEADDDDEDEDGDEVEEEAEPEYEATERTTTSIATTTTTTTESVEEVVR----- 288
      :||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| |||
Db    241 DEDADDD-DDDDGDEI-EETEEYEATERTTTSIATTTTTTTESVEEVVREVCSEQAETG 298

Qy    289 -----VPTTAASTPDAVDK 302
      :||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    299 PCRAMISRWFYDVAEGKCAPFFYGGCGGNRNNFDSEEYCMVCGSVLPTTAASTPDAVDK 358

Qy    303 YLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHFQE 362
      ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    359 YLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHFQE 418

Qy    363 KVESLEQEAANERQQLVETHMARVEAMLNDRRRRLALENYITALQAVPPRPRHVFNMLKKY 422
      ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    419 KVESLEQEAANERQQLVETHMARVEAMLNDRRRRLALENYITALQTVPPRPRHVFNMLKKY 478

Qy    423 VRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLYNVPAVAEE 482
      ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    479 VRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLYNVPAVAEE 538

Qy    483 IQDEVDELLQKEQNYSDDLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSLDD 542
      ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    539 IQDEVDELLQKEQNYSDDLANMISEPRISYGNDALMPSLTETKTTVELLPVDGEFSLDD 598

Qy    543 LQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEFRH 602
      ||||| ||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    599 LQPWHPFGVDSVPANTENEVEPVDARPAADRGLTTRPGSGLTNVKTEEVSEVKMDAEFRH 658

Qy    603 DSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGVVE 662
      ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
```



Db 659 DSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHG VVE 718

Qy 663 VDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695  
 |||  
 Db 719 VDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 751

RESULT 3

Q98SG0

ID Q98SG0 PRELIMINARY; PRT; 693 AA.  
 AC Q98SG0;  
 DT 01-JUN-2001 (TrEMBLrel. 17, Created)  
 DT 01-JUN-2001 (TrEMBLrel. 17, Last sequence update)  
 DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)  
 DE Beta-amyloid precursor protein A.  
 GN APP.  
 OS Xenopus laevis (African clawed frog).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Amphibia; Batrachia; Anura; Mesobatrachia; Pipoidae; Pipidae;  
 OC Xenopodinae; Xenopus.  
 OX NCBI\_TaxID=8355;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RA Van den Hurk W.H.;  
 RL Thesis (2001), Department of Biological Sciences,  
 RL University of Nijmegen, Nijmegen, Netherlands.  
 DR EMBL; AJ298150; CAC37193.1; -.  
 DR HSSP; P05067; 1HZ3.  
 DR GO; GO:0016020; C:membrane; IEA.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 KW Signal.  
 FT SIGNAL 1 18 POTENTIAL.  
 SQ SEQUENCE 693 AA; 78568 MW; CAF1DF655C1AB653 CRC64;

Query Match 88.0%; Score 3214; DB 13; Length 693;  
 Best Local Similarity 87.8%; Pred. No. 4.8e-185;  
 Matches 612; Conservative 36; Mismatches 43; Indels 6; Gaps 4;

Qy 1 MLPGIALLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60  
 ||| : ||:| | |||| ||| ||||| :||| :|||  
 Db 1 MLPHITLLVLTV-GALALEVPADGNGGLLAEPQIAMFCGKLNMHMNVQNGKWETDVSGTK 59

Qy 61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120  
 || ||||| :||| :| | :|||  
 Db 60 GCIGTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKKGRKQCKSRTHIVVPYRCLVG 119

Qy 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180  
 ||||| :||| :||| :||| :|||  
 Db 120 EFVSDALLVPDKCKFLHQERMDICETHLHWHTVAKESCSEKSMLEHYGMLLPCGIDKFR 179

Qy 181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVA--EEEEVAEVE 238  
 ||||| ||||: |||| |||| |||| || ||: || || |||| |||  
 Db 180 GVEFVCCPSAEESFSADSADA-EDDSDAWVGADADYVDRSDDKAVEAQPDEEEVVEVE 238  
 Qy 239 EEEADDEDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPD 298  
 ||| |||| |||| ||| |||| |||| |||| |||| |||| |||| |||| |||| ||||  
 Db 239 EEETDDDED--DGDEAEPEPEPYEEATERTTSIATTTTTTTTESVEEVVRVPATAASTPD 296  
 Qy 299 AVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAEERQAKNLPKADKKAVIQ 358  
 ||||| | |||| | ||||| ||||: ||: ||: ||||| ||||| ||||| |||||  
 Db 297 AVDKYLENPNDENEHDFLKAKERLEGKHKREKMSEVMKEWEAEERQAKNLPKADKKAVIQ 356  
 Qy 359 HFQEKVESLEQEAAANERQQVLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNM 418  
 ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||  
 Db 357 HFQEKVESLEQEAAANERQQVLVETHMARVEAMLNDRRIAENYITALQADPPRPRHVFNM 416  
 Qy 419 LKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVA 478  
 ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||  
 Db 417 LKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVINERMNQSFSLLYKVA 476  
 Qy 479 VAEIQDEVDDELLQKEQNYSDVLNMISEPRISYGNLMPSLTETKTTVELLPVNGEF 538  
 ||||| ||||| ||||| ||||: ||: ||: ||: ||||| ||||| ||||| ||||| |||||  
 Db 477 VAEIQDEVDDELQKEQNYSDVMVSNMVSDFRVSYGNLMPSLSETKTTVELLPVDGEF 536  
 Qy 539 SLDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDA 598  
 ::||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||  
 Db 537 NIEDLQPWHSFGVDSVPANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDS 596  
 Qy 599 EFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHH 658  
 |:| |:| ||||| ||||: ||||| ||||| ||||| ||||| ||||| ||||| |||||  
 Db 597 EYRHTAYEVHHQKLVFFAEEVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTTIHH 656  
 Qy 659 GVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695  
 ||||| ||||: ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||  
 Db 657 GVVEVDAAVTPEERHLTKMQQNGYENPTYKFFEQMQN 693

# RESULT 4

Q98SF9

ID Q98SF9 PRELIMINARY; PRT; 695 AA.

AC Q98SF9;

DT 01-JUN-2001 (TrEMBLrel. 17, Created)

DT 01-JUN-2001 (TrEMBLrel. 17, Last sequence update)

DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)

DE Beta-amyloid precursor protein B.

GN APP.

OS *Xenopus laevis* (African clawed frog).

OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

OC Amphibia; Batrachia; Anura; Mesobatrachia; Pipoidea; Pipidae;

OC Xenopodinae; *Xenopus*.

OX NCBI\_TaxID=8355;

RN [1]

RP SEQUENCE FROM N.A.

RA Van den Hurk W.H.;

RL Thesis (2001), Department of Biological Sciences,

RL University of Nijmegen, Nijmegen, Netherlands.

DR EMBL; AJ298151; CAC37194.1; -.  
DR HSSP; P05067; 1HZ3.  
DR GO; GO:0016020; C:membrane; IEA.  
DR InterPro; IPR008155; A4\_APP.  
DR InterPro; IPR008154; A4\_extra.  
DR InterPro; IPR001255; Beta-APP.  
DR Pfam; PF02177; A4\_EXTRA; 1.  
DR Pfam; PF03494; Beta-APP; 1.  
DR PRINTS; PR00203; AMYLOIDA4.  
DR SMART; SM00006; A4\_EXTRA; 1.  
DR PROSITE; PS00319; A4\_EXTRA; 1.  
DR PROSITE; PS00320; A4\_INTRA; 1.  
KW Signal.  
FT SIGNAL 1 18 POTENTIAL.  
SQ SEQUENCE 695 AA; 78803 MW; DC14EB02AFB0204A CRC64;

Query Match 87.4%; Score 3190; DB 13; Length 695;  
Best Local Similarity 87.2%; Pred. No. 1.3e-183;  
Matches 609; Conservative 39; Mismatches 44; Indels 6; Gaps 5;

Qy 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60  
||| : ||:| | | |||| | | ||||| |||||:|||||:| ||||  
Db 1 MLPHITLLVLTA-GALALEVPADGNGLLAEPQIAMFCGKLNMHMNVQNGKWETDVSGTK 59  
  
Qy 61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120  
|| ||||| |||||:|||||: | |:|||||  
Db 60 GCIGTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKKGRKQCKSRTHIVVPYRCLVG 119  
  
Qy 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180  
||||| |||||:|||||:||||| :||:|||||  
Db 120 EFVSDALLVPDKCKFLHQERMDICETHLHWHTVAKESCSEKIMSLHEYGMLLPCGIDKFR 179  
  
Qy 181 GVEFVCCPLAEESDNVDSADAEDDSVWVGADTDYADGSEDKVVEV--AEEEEVAEVE 238  
||||| ||||:| |||| | ||||| || | |:| | |||| |||  
Db 180 GVEFVCCPTAEESFSADSADA-EDDSVWVGADADYVDRSDDKAQVEEEEEVEVE 238  
  
Qy 239 EEEADDDDEDGEDGEVEEEAEPEYEEATERTTTSIATTTTTTTSVEEVVR-VPTTAASTP 297  
||||| |:| ||| | | ||||| ||||| || || |||  
Db 239 EEEADDD-DEDDGDETEEEPEEPEYEEATERTTTSIATTTTTTTSVEEVVRVAVPATAVSTP 297  
  
Qy 298 DAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVI 357  
||||| | |||| | ||||| ||||:|:|:| ||||| |||||  
Db 298 DAVDKYLENPNDENEHDFLKAKEKLEKHKREKMSQVMKEWEEAERQAKNLPKADKKAVI 357  
  
Qy 358 QHFQEKVESLEQEAAANERQQLVETHMARVEAMLNDRRRLALENYITALQAVPPRPRHVFN 417  
||||| |||||:||||| |||||  
Db 358 QHFQEKVESLEQEAAANERQQLVETHMARVEATLNDRRRLALENYITALQADPPRPRHVFN 417  
  
Qy 418 MLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVP 477  
||||| ||||| |||||  
Db 418 MLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVINERMNQSFSLLYKVP 477  
  
Qy 478 AVAEELIQDEVDELLQKEQNYSDVLNMISEPRISYGNLMPSLTETKTTVELLPVNGE 537  
||||| |||||:|:|:| |:| |||||:|||||:|  
Db 478 AVAEELIQDEVDELFQKEQNYSDVMVSNMVS DHRVSYGNLMPSLSETKTTVELLPVDGE 537  
  
Qy 538 FSLDDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVKMD 597

```

      |:::||||||| ||||||||||||||||||||||||||||||||||| |||||||
Db      538 FNVEDLQPWHSFGVDSVPANTENEVEPVDARPAADRGLTTRPGSGLTNIKREEISEVKMD 597

Qy      598 AEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIH 657
      |:|:|:|: |||||||||||:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|
Db      598 SEYRHDAAYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTTIH 657

Qy      658 HGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
      |||||||||||:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|
Db      658 HGVVEVDAAVTPEERHLTKMQQNGYENPTYKFFEQMQN 695

```

RESULT 5

Q7ZXQ0

```

ID   Q7ZXQ0          PRELIMINARY;          PRT;          695 AA.
AC   Q7ZXQ0;
DT   01-JUN-2003 (TrEMBLrel. 24, Created)
DT   01-JUN-2003 (TrEMBLrel. 24, Last sequence update)
DT   01-OCT-2003 (TrEMBLrel. 25, Last annotation update)
DE   Hypothetical protein.
OS   Xenopus laevis (African clawed frog).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Amphibia; Batrachia; Anura; Mesobatrachia; Pipoidae; Pipidae;
OC   Xenopodinae; Xenopus.
OX   NCBI_TaxID=8355;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   TISSUE=Embryo;
RA   Klein S., Strausberg R.;
RL   Submitted (JAN-2003) to the EMBL/GenBank/DDBJ databases.
DR   EMBL; BC044324; AAH44324.1; -.
DR   GO; GO:0016020; C:membrane; IEA.
DR   InterPro; IPR008155; A4_APP.
DR   InterPro; IPR008154; A4_extra.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF02177; A4_EXTRA; 1.
DR   Pfam; PF03494; Beta-APP; 1.
DR   PRINTS; PR00203; AMYLOIDA4.
DR   SMART; SM00006; A4_EXTRA; 1.
DR   PROSITE; PS00319; A4_EXTRA; 1.
DR   PROSITE; PS00320; A4_INTRA; 1.
KW   Hypothetical protein.
SQ   SEQUENCE 695 AA; 78803 MW; C1BD8AACC3356B05 CRC64;

```

```

Query Match          87.3%; Score 3188; DB 13; Length 695;
Best Local Similarity 87.2%; Pred. No. 1.8e-183;
Matches 609; Conservative 38; Mismatches 45; Indels 6; Gaps 5;

```

```

Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
      ||| : ||:| | | |||| | | |||||||:|:|:|:|:|:|:|:|:|:|:|:|:|
Db      1 MLPHITLLVLTA-GALALEVPADGNGGLLAEPQIAMFCGKLNMHMNVQNGKWETDVSGTK 59

Qy      61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120
      || |||||||:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|
Db      60 GCIGTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKKGRKQCKSRTHIVVPYRCLVG 119

Qy      121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

```



RA Okado H., Okamoto H.;  
 RT "A Xenopus homologue of the human beta-amyloid precursor protein:  
 RT developmental regulation of its gene expression.";  
 RL Biochem. Biophys. Res. Commun. 189:1561-1568(1992).  
 DR EMBL; S52417; AAB24853.1; -.  
 DR HSSP; P05067; 1HZ3.  
 DR GO; GO:0016020; C:membrane; IEA.  
 DR GO; GO:0004867; F:serine protease inhibitor activity; IEA.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR InterPro; IPR002223; Kunitz\_BPTI.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR Pfam; PF00014; Kunitz\_BPTI; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR PRINTS; PR00759; BASICPTASE.  
 DR ProDom; PD000222; Kunitz\_BPTI; 1.  
 DR SMART; SM00131; KU; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 DR PROSITE; PS00280; BPTI\_KUNITZ\_1; 1.  
 DR PROSITE; PS50279; BPTI\_KUNITZ\_2; 1.  
 KW Protease inhibitor; Serine protease inhibitor.  
 SQ SEQUENCE 747 AA; 84893 MW; A75E81885681D948 CRC64;

Query Match 85.0%; Score 3103; DB 13; Length 747;  
 Best Local Similarity 81.0%; Pred. No. 2.5e-178;  
 Matches 598; Conservative 35; Mismatches 41; Indels 64; Gaps 5;

Qy	17	ALEVPTDGNAGLLAEPQIAMF-CGRLNMHMNVQNGKWSDPSGTKTCIDTKEGILQYCQE	75
		::	
Db	15	ALEVLVDGNGGLLAEPQIAMFSVARLNMHMNVQNGKWETDVSG---CIGTKEGILQYCQE	71
Qy	76	VYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVGFEFVSDALLVPDKCKF	135
		:     :    :	
Db	72	VYPELQITNVVEANQPVTIQNWCKKGRKQCKSRTHIVVPYRCLVGFEFVSDALLVPDKCKF	131
Qy	136	LHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEFVCCPLAEESDN	195
		:           :      :  :                      ::	
Db	132	LHQERMDICETHLHWHTVAKESCSEKSMSLHEYGMLLPCGIDKFRGVEFVCCPSAEES	191
Qy	196	VDSADAEEDSDVWVGADTDYADGSEDKVVEVA---EEEEVAEVEEEEADDDDEDGDGDE	253
		:	
Db	192	FDSADAEEDDCDVWVGADADYVDRSDDKAVEAQPDEEEVVEVEEEEETDDDED--DGDE	249
Qy	254	VEEEAEEPVEEATERTTTSIATTTTTTTESVEEVVR-----	288
Db	250	AEEPEEPVEEATERTTTSIATTTTTTTESVEEVVREVCSEQAETGPCRAMISRWYDVTE	309
Qy	289	-----VPTTAASTPDAVDKYLETPGDENEHAHFQ	317
		:	
Db	310	SKCAQFIYGGCGGNRRNFESDDYCMVCGSVIPATAASTPDAVDKYLENPDENEDRFL	369
Qy	318	KAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHFQEKVESLEQEAANERQQ	377
		:  :  :                           :	
Db	370	KAKERLEGKHREKMSEVMKEWEAERQAKNLPKADKKAVIQHFQEKVESLEQEAQORQQ	429







Db 656 OYTSIH HGVVEVDAAVTPEERHLSKMOONGYENPTYKFFEOMON 699

## RESULT 8

O9PVL1

```

ID      Q9PVL1      PRELIMINARY;      PRT;      569 AA.
AC      Q9PVL1;
DT      01-MAY-2000 (TrEMBLrel. 13, Created)
DT      01-MAY-2000 (TrEMBLrel. 13, Last sequence update)
DT      01-JUN-2003 (TrEMBLrel. 24, Last annotation update)
DE      Amyloid protein (Fragment).
GN      APP.
OS      Gallus gallus (Chicken).
OC      Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC      Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;
OC      Gallus.
OX      NCBI_TaxID=9031;
RN      [1]
RP      SEQUENCE FROM N.A.
RC      TISSUE=Brain;
RA      Coulson E.J., Paliga K., Beyreuther K., Masters C.L.;
RT      "What the evolution of the amyloid protein precursor supergene family
RT      tells us about its function.";
RL      Neurochem. Int. 0:0-0(2000).
DR      EMBL; AF030341; AAF12698.1; -.
DR      HSSP; P05067; 1BA4.
DR      GO; GO:0016020; C:membrane; IEA.
DR      InterPro; IPR008155; A4_APP.
DR      InterPro; IPR008154; A4_extra.
DR      InterPro; IPR001255; Beta-APP.
DR      Pfam; PF02177; A4_EXTRA; 1.
DR      Pfam; PF03494; Beta-APP; 1.
DR      PRINTS; PR00203; AMYLOIDA4.
DR      PROSITE; PS00319; A4_EXTRA; 1.
DR      PROSITE; PS00320; A4_INTRA; 1.
FT      NON_TER      1      1
SQ      SEQUENCE      569 AA: 64753 MW: 0AB8BB851863A19D CRC64:

```

Query Match 75.8%; Score 2767.5; DB 13; Length 569;  
Best Local Similarity 93.5%; Pred. No. 2.6e-158;  
Matches 535; Conservative 14; Mismatches 18; Indels 5; Gaps 4;

Qy	126	ALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEFV	185
		:	
Db	1	ALLVPDKCKLLHQERMDVCETHLHWHTVAKESCSEKSMNLHDYGMLLSCGIDKFRGVEFV	60
Qy	186	CCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVE--VAEEEEVAEVEEEAD	243
		:       :             :         :    :    :    :	
Db	61	CCPLAEESDNLDSADAEEDDSVWVGADADYADGSDDKVVEEQPEEDEELTVVEDEDAD	120
Qy	244	DDEDDGDGEVEEEAEPEYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAVDKY	303
		:      :	
Db	121	DD-DDDDGDEI-EETEEYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDVVDKY	178
Qy	304	LETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHFQEK	363
Db	179	LETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHFOEK	238

Qy 364 VESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKYV 423  
 |||:|||||  
 Db 239 VESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQTVPPRPRHVFNMLKKYV 298  
 Qy 424 RAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAAVEEI 483  
 |||:|||||  
 Db 299 RAEQKDRQHTLKHFEHVRMVDPKKAVQIRSQVMTHLRVIYERMNQSLSLFLYNVPAAVEEI 358  
 Qy 484 QDEVDELLQKEQNYSDVLNMISEPRISYGN DALMP SLTETKTTVELLPVNGEFSLDDL 543  
 |||:|||||  
 Db 359 QDEVDELLQKEQNYSDVLNMISEPRISYGN DALMP TLTETKTTVELLPVVG EFSLDDL 418  
 Qy 544 QPWSHF'GADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEFRHD 603  
 |||:|||||  
 Db 419 QPWHFPGVDSVPANTENEVEPV DARPAADRGLTTRPGSGLTNVKTEEVSEVKMDAEFRHD 478  
 Qy 604 SGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIH HGVVEV 663  
 |||:|||||  
 Db 479 SGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIANVIVITLVMLKKKQYTSIH HGVVEV 538  
 Qy 664 DAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695  
 |||:|||||  
 Db 539 DAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 569

RESULT 9

O93296

ID O93296 PRELIMINARY; PRT; 534 AA.  
 AC O93296;  
 DT 01-NOV-1998 (TrEMBLrel. 08, Created)  
 DT 01-NOV-1998 (TrEMBLrel. 08, Last sequence update)  
 DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)  
 DE Amyloid protein (Fragment).  
 OS Gallus gallus (Chicken).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;  
 OC Gallus.  
 OX NCBI\_TaxID=9031;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RX MEDLINE=98337885; PubMed=9671674;  
 RA Barnes N.Y., Li L., Yoshikawa K., Schwartz L.M., Oppenheim R.W.,  
 RA Milligan C.E.;  
 RT "Increased production of amyloid precursor protein provides a  
 RT substrate for caspase-3 in dying motoneurons."  
 RL J. Neurosci. 18:5869-5880(1998).  
 DR EMBL; AF042098; AAC25052.1; -.  
 DR HSSP; P05067; 1BA4.  
 DR GO; GO:0016020; C:membrane; IEA.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.

DR PROSITE; PS00320; A4\_INTRA; 1.

FT NON TER 1 1

SQ SEQUENCE 534 AA; 60597 MW; FB53ECC2E66D4C92 CRC64;

Query Match 71.6%; Score 2613; DB 13; Length 534;

Best Local Similarity 94.8%; Pred. No. 4.7e-149;

Matches 506; Conservative 13; Mismatches 11; Indels 4; Gaps 3;

```
Qy      164 NLHDYGMLLPCGIDKFRGVEFVCCPLAEESDNVDSADAEEDDSDVWVGADTDYADGSED 223
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db       3  NLHDYGMLLPCGIDKFRGVEFVCCPLAEESDNLDSADAEEDDSDVWVGADADYADGSDD 62

Qy      224 KVVE--VAEEEEVAEEEEEEADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTE 281
          |||||  |:|:|:  ||:|:||||  |:|:|:|  ||  ||  |||:|||||
Db       63 KVVVEEQPEEDEELTVVEDEDADDD-DDDDGDEI-EETEEYEEATERTTSIATTTTTTTE 120

Qy      282 SVEEVVRVPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEA 341
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||
Db      121 SVEEVVRVPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEA 180

Qy      342 ERQAKNLPKADKKAVIQHFQEKVESLEQEANERQQLVETHMARVEAMLNDRRRLALENY 401
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||
Db      181 ERQAKNLPKADKKAVIQHFQEKVESLEQEANERQQLVETHMARVEAMLNDRRRIALENY 240

Qy      402 ITALQAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRV 461
          |||||  |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||
Db      241 ITALQTVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRV 300

Qy      462 IYERMNQSLSLYNVPAVAEEIQDEVDELLQKEQNYSDDVLANMISEPRISYGNDALMPS 521
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||
Db      301 IYERMNQSLSFLYNVPAVAEEIQDEVDELLQKEQNYSDDVLANMISEPRISYGNDALMPS 360

Qy      522 LTETKTTVELLPVNGEFSLDDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGS 581
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||
Db      361 LTETKTTVELLPVDGEFSLDDLQPWHPFGVDSVPANTENEVEPVDPARPAADRGLTTRPGS 420

Qy      582 GLTNIKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVI 641
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||
Db      421 GLTNVKTEEVSEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVI 480

Qy      642 VITLVMLKKKQYTSIHHGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||
Db      481 VITLVMLKKKQYTSIHHGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 534
```

#### RESULT 10

Q7ZZT1

ID Q7ZZT1 PRELIMINARY; PRT; 678 AA.

AC Q7ZZT1;

DT 01-JUN-2003 (TrEMBLrel. 24, Created)

DT 01-JUN-2003 (TrEMBLrel. 24, Last sequence update)

DT 01-OCT-2003 (TrEMBLrel. 25, Last annotation update)

DE Amyloid protein a variant 2.

GN APPA.

OS Brachydanio rerio (Zebrafish) (Danio rerio).

OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

OC Actinopterygii; Neopterygii; Teleostei; Ostariophysi; Cypriniformes;

OC Cyprinidae; Danio.  
 OX NCBI\_TaxID=7955;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RA Groth C., Lardelli M.;  
 RT "Investigation of zebrafish appa expression during embryogenesis."  
 RL Submitted (APR-2003) to the EMBL/GenBank/DDBJ databases.  
 DR EMBL; AY271746; AAP22958.1; -.  
 DR GO; GO:0016020; C:membrane; IEA.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 SQ SEQUENCE 678 AA; 76755 MW; 94163778444FD0BC CRC64;

Query Match 70.3%; Score 2567; DB 13; Length 678;  
 Best Local Similarity 72.0%; Pred. No. 3.7e-146;  
 Matches 499; Conservative 78; Mismatches 94; Indels 22; Gaps 11;

Qy	5	LALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGKTCTCID	64
		:  :  :   :  :        :   :  :  :     :  :	
Db	6	LFILLMAVASTLAVEVPSDSGTGLLAEPQIAMFCGKLMHINIQSGKWEPPSGSKSCIG	65
Qy	65	TKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVGEFVS	124
		:   :  :  :     :    :    :	
Db	66	NKEGILQYCQEVYPELQITNVVEANQPVSIWDWCKKSRKQCRSHMHIVPYRCLVGEFVS	125
Qy	125	DALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEF	184
		:  :  :    :    :    :    :	
Db	126	DALLVPDKCKFLHQERMDMCESHLHWHTVAKESCGDRSMNLHDYGMLLPCGIDRFRGVEF	185
Qy	185	VCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEEADD	244
		: :         :   :  : :    :  :	
Db	186	VCCP-ADAGKESESAAVEEDSDVWVGGAEDYTENSMTR--DAAAEPAV--LEDDEDAD	240
Qy	245	DEDDDEDG-DVEEEAEPEYEEATERTT-SIATTTTTTTESVEEVVRVPTTAASTPDAVDK	302
		:  :      : :        :  : : :    :    :    :	
Db	241	EEDEDGDGDRDEKIEEEEEERTQSTSAALTSTTTTTTESVEEVVRVPTPSSSPDAVDR	300
Qy	303	YLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHFQE	362
		:    :    :	
Db	301	YLETPADENEHAHFLKAKESLETKHRERMSQVMREWEEAERQAKSLPRNDKKAVIQHFQE	360
Qy	363	KVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKY	422
		:     :  :    :    :    :    :    :	
Db	361	KVEALEQESASERQQLVETHMARVEALLNDRRLALESYLSALQADPPRPRHVFSLKKY	420
Qy	423	VRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPVAEE	482
		:    :    :    :    :    :    :	
Db	421	VRAEQKDRQHTLKHFEHVRMVDPKKAAQIRPQVLTHLRVIEERMNQSLGLLYKVPGVADD	480
Qy	483	IQDEVDELLQKEQNYSDDLANMISEPRISYGNLDMPSLTETKTTVELLPVNGEFLDD	542



Query Match 69.3%; Score 2529; DB 13; Length 738;  
Best Local Similarity 66.4%; Pred. No. 8e-144;  
Matches 501; Conservative 79; Mismatches 90; Indels 84; Gaps 14;

```
Qy      5 LALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTKTCID 64
      | :||:| : |:||:| | ||||| |||||:||||:|:|:|:| ||||:|:|
Db      6 LFILLMAVASTLAVEVPSDSGTGLLAEPQIAMFCGKLNMHINIQSGKWEPPSGSKSCIG 65

Qy     65 TKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVGEFVS 124
      | ||||| ||||| ||||| |||||:| :||:| ||||:| | | :||| |||||
Db     66 NKEGILQYCQEVYPELQITNVVEANQPVSIWDWCKKSRKQCRSHMHIVPYRCLVGEFVS 125

Qy    125 DALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEF 184
      | ||||| ||||| ||||| |||||:| :||:| ||||| |||||:| |||||
Db    126 DALLVPDKCKFLHQERMDMCESHLHWHTVAKESCGDRSMNLHDYGMLLPCGIDRFRGVEF 185

Qy    185 VCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEEADD 244
      ||| | : :|| | ||||| |||||:| | : | : : | | | :|:|:|
Db    186 VCCP-ADAGKESESAAVEEDSDVWWGGAEADYTENSMTR--DAAAEPAVLE-DDEDADE 241

Qy    245 DED-DEDGD-----EVEEEAEEPYEEATERTT-SIATTTTTTTESVEEVVR----- 288
      :|| |:|| :||| || || | : | : : : ||||| |||||
Db    242 EEDEDQDGDGRDEKIEEEEE--EERTQSTSAALTSTTTTTTESVEEVVREVCFASAET 299

Qy    289 -----VPTTAASTPDAVD 301
      :|| :|| ||||
Db    300 GPCRAML SRWYYVREERRCAPFIYGGCGGNRNNFEESEYCLSVCSGVLPTPSSSPDAVD 359

Qy    302 KYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHFQ 361
      :||| | ||||| |||| | | ||||| ||||| |||||:|:| |||||
Db    360 RYLETPADENEHAHFLKAKESLETKHRERMSQVMREWEAAERQAKSLPRNDKKAVIQHFQ 419

Qy    362 EKVESLEQEAANERQQVLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKK 421
      ||||:||||:|:||||| |||||:||||| |||||:|:| |||||:|:|
Db    420 EKVEALEQESASERQQVLVETHMARVEALLNDRRLALESYLSALQADPPRPRHVFSLKK 479

Qy    422 YVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVAE 481
      | ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    480 YVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRPQVLTHLRVIEERMNQSGLLYKVPGVAD 539

Qy    482 EIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSLD 541
      :|||:| ||||:| ||||:| ||||:| ||||:| ||||:| ||||:|
Db    540 DIQDQV-ELLQREQQEMSAQLANLQSDARVSYGNDAIMPST--AGLELLPAEDTQGF 595

Qy    542 DLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEFR 601
      : | | | | | :||| || | | ||| || | :| | :|:| | |
Db    596 FIHP-ESFN----QPNTNQVEPVDARVPDLDLATRPVSGL---KPDDIPELRMEAEER 647

Qy    602 HDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHG 661
      | | :||| ||||| ||||| |||||:|||||:||||| |||||:|
Db    648 HS---EVYHQKLVFFAEDVSSNKGAIIGLMVGGVVIATIIIVITLVMLRKKQYTSIHG 704

Qy    662 EVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
      | ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    705 EVDAAVTPEERHLSKMQQNGYENPTYKFFEQMHN 738
```

RESULT 12

Q8UUR9

ID Q8UUR9 PRELIMINARY; PRT; 694 AA.  
AC Q8UUR9;  
DT 01-MAR-2002 (TrEMBLrel. 20, Created)  
DT 01-MAR-2002 (TrEMBLrel. 20, Last sequence update)  
DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)  
DE Putative membrane protein.  
GN APPB.  
OS Brachydanio rerio (Zebrafish) (Danio rerio).  
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
OC Actinopterygii; Neopterygii; Teleostei; Ostariophysi; Cypriniformes;  
OC Cyprinidae; Danio.  
OX NCBI\_TaxID=7955;  
RN [1]  
RP SEQUENCE FROM N.A.  
RC TISSUE=Brain;  
RX PubMed=11862463;  
RA Musa A., Lehrach H., Russo V.E.A.;  
RT "Distinct expression patterns of two zebrafish homologues of the human  
RT APP gene during embryonic development."  
RL Dev. Genes Evol. 211:563-567(2001).  
DR EMBL; AJ315639; CAC85736.1; -.  
DR ZFIN; ZDB-GENE-020220-1; appb.  
DR GO; GO:0016020; C:membrane; IEA.  
DR InterPro; IPR008155; A4\_APP.  
DR InterPro; IPR008154; A4\_extra.  
DR InterPro; IPR001255; Beta-APP.  
DR Pfam; PF02177; A4\_EXTRA; 1.  
DR Pfam; PF03494; Beta-APP; 1.  
DR PRINTS; PR00203; AMYLOIDA4.  
DR SMART; SM00006; A4\_EXTRA; 1.  
DR PROSITE; PS00319; A4\_EXTRA; 1.  
DR PROSITE; PS00320; A4\_INTRA; 1.  
SQ SEQUENCE 694 AA; 79228 MW; 2B03382D411162DC CRC64;

Query Match 68.1%; Score 2487.5; DB 13; Length 694;  
Best Local Similarity 67.9%; Pred. No. 2.3e-141;  
Matches 477; Conservative 98; Mismatches 97; Indels 31; Gaps 9;

Qy	7	LLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLLNMHMNVQNGKWDSDPSGKTCTCIDTK	66
		: : :    : :      :    :    :    :   :    :	
Db	9	LLLMLTTLSIAIEVPSDDSVGLLAEPQVAMFCGKLNMHINVQSGKWEPTDPTGKSCISTK	68
Qy	67	EGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVGEFVSDA	126
		:      :       :        : :      :	
Db	69	EGILKYCQEVYPDLQITNVVEANQPVSIQNWCKMGRRCRSHTHIVVPYRCLVGEFVSDA	128
Qy	127	LLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEFVC	186
		:       : : :       :  :       :	
Db	129	LLVPDKCKFLHQERMDMCESHLHWHTVAKESCGDRSMNLHDYGMLLPCGIDRFRGVEFVC	188
Qy	187	CPLAEESDNVDSADAEEDSDVWVGADTDYADGS--EDKVV-----EVAEEEEVAEVEE	239
		:  :  :   :    :      : :      :::     :	
Db	189	CPMEEQKD-LDSEEQEEANSVWVGGAETETDASVLKEQVTAKPDPAVTEDEDEDLNNEE	247

Qy	240	EEADDDDEDDGDGEVEEEAAEE-----PYEEATERTTT--TTTTTTTSEVEEVVRVPTT	292
Db	248	EEVWDNDEDDGDGEDDEDEEDDDDEDIIDEQDTSEQTSNIAMTTTTTTTTTESIEEVVRVPTM	307
Qy	293	AASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKAD	352
Db	308	APSPADAVDRYLEAPGDMNEHMRFAQKAKESLEAKHREKMSQVMREWEEAERQAKNLPKAD	367
Qy	353	KKAVIQHFQEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRP	412
Db	368	KKTIIQRFQEKVESLEKEAAGERQQLVETHMARVEALLNDRRRQALESYLSSLQSDQPRP	427
Qy	413	RHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSL	472
Db	428	RQVLNLLKKYIRAEQKDRQHTLKHFEHVRMVDPKKAAQIRPFVMTLHRLVIEERMNQSLSL	487
Qy	473	LYNVPAAVEEIQDEVDLQKEQNYSDVLNLMISEPRISYGNLALMPSLTETKTTVELL	532
Db	488	LYKVPQVANDIQDQVAVLVQRDQAEVTQQLSSLQSKMRVSYGNLALMPDLDPDSTPLDNL	547
Qy	533	PVNGEFLDDLQPWHSFGADSVFANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEIS	592
Db	548	PPEQD-GLGFIHP-ESFN-----QANTDNHVEPVDARPIPERGLPTRP-----EIP	591
Qy	593	EVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQ	652
Db	592	KVRLDIEERHNAGYDVRDKRLMFLAEDMGSNKGAIIGLMVGGVVIATVIVITLVMLRKKQ	651
Qy	653	YTSIHGHVVEVDAAVTPEERHLSKMQONGYENPTYKFFEQMQN	695
Db	652	YTSIHGHVIEVDAAVTPEERHLAKMQONGYENPTYKFFEQMQN	694

## RESULT 13

Q9I9E7

ID Q9I9E7 PRELIMINARY; PRT; 612 AA.

AC Q9I9E7;

DT 01-OCT-2000 (TrEMBLrel. 15, Created)

DT 01-OCT-2000 (TrEMBLrel. 15, Last sequence update)

DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)

DE Amyloid protein (Fragment).

GN APPA.

OS Brachydanio rerio (Zebrafish) (Danio rerio).

OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

OC Actinopterygii; Neopterygii; Teleostei; Ostariophysi; Cypriniformes;

OC Cyprinidae; Danio.

OX NCBI TaxID=7955;

RN [1]

RP SEQUENCE FROM N.A.

RA Slavov D.B., Gardiner K.;

RT "An App cDNA from Zebrafish (*Danio rerio*).";

RL Submitted (APR-2000) to the EMBL/GenBank/DDBJ databases.

DR EMBL; AF257742; AAF71748.1; -.

DR HSSP; P05067; 1HZ3.

DR ZFIN: ZDB-GENE-000616-13; appa.

DR GO: GO:0016020; C:membrane; IEA.

DR InterPro; IPR008155; A4 APP.





## O8BPC7

Query Match 52.8%; Score 1928; DB 11; Length 384;  
Best Local Similarity 98.2%; Pred. No. 4.7e-108;  
Matches 377; Conservative 2; Mismatches 5; Indels 0; Gaps 0;

Qy	312 EHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHFQEKVESLQEQA	371 
Db	1 EHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHFQEKVESLQEQA	60
Qy	372 ANERQQLVETHMARVEAMLNDRRRLALENYITALQAVPPRPHVFNMLKKYVRAEQKDRQ	431 
Db	61 ANERQQLVETHMARVEAMLNDRRRLALENYITALQAVPPRPHHVFNFNLKKYVRAEQKDRQ	120
Qy	432 HTLKHFHEVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPVAEELIODEVDELL	491 
Db	121 HTLKHFHEVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPVAEELIODEVDELL	180
Qy	492 QKEQNYSDDVLANMISEPRISYGNDALMPSTETKTTVELLPVNGEFLDDLQPWHFSGA	551   ::
Db	181 QKEQNHSDDLANMISEPRISYGNDALMPSTETKTTVELLPVNGEFLDDLQPWHFFGV	240
Qy	552 DSVPAENTENEVEPDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEFRHDGSYEIVHHQ	611   :::



```

      ||||| ||||:|:| | |:|:| | | |||| | | : | : |||||:
Db      133 CLVGEFVSDVLLVPEKCQFFHKERMEVCENHQHWHTVVKEACLTQGMTLYSYGMLLPCGV 192
Qy      177 DKFRGVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAE 236
      |:| | |:| | : :| : ||: : : | | | :| |:
Db      193 DQFHGTEYVCCPQTKIIGSVSKEEEEEDEE-----EEEEDEEEDYDVYKSEFPTEAD 245
Qy      237 VEE--EEA--DDDEDDGDEVEEEAE-----EPYEEATERTTSIATTTTTTTESVE 284
      |:| | | :| | |:|:| |:| : : | | | | : | : : :
Db      246 LEDFTEAAVDEDEDEEEGEEVVEDRDYYYDTFKGDDYNE--ENPTEPGSDGTMSDKEIT 303
Qy      285 EVVRVPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQ 344
      |:| | | | | | | | |:| | | | | | | | | |:| | | | | |
Db      304 HDVKVPPTPLPTND-VDVYFETSADDNEHARFQKAKEQLEIRHRNRMDRVKKEWEEAELQ 362
Qy      345 AKNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITA 404
      |||||: : :| | | |:|:| |:|:| |:|:| |:|:| |:|:| |:|:| |
Db      363 AKNLPKAERQTLIQHFQAMVKALEKEAASEKQQLVETHLARVEAMLNDRRMALENYLAA 422
Qy      405 LQAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYE 464
      ||: | | | : | :| | | | | | | | | | | | | | | | | | |
Db      423 LQSDPPRPHRILQALRRYVRAENKDRLHTIRHYQHVLAVDPEKAAQMKSQVMTHLHVIEE 482
Qy      465 RMNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTE 524
      | | | | | | | | | | |:| |:| |:| |:| |:| |:| |:| |:|
Db      483 RRNQSLSLLYKVPYVAQEIQEEIDELLQEQR-----ADM-----DQFTASISE 525
Qy      525 TKTTVELLPVNGEFSLDDLQPWHSFGADSVANTENEVEFPVDARPAADRGL----- 575
      | | | | | |:| | | : : | | | | | | | | | | : | | |
Db      526 TPVDVR---VSSEES-EEIPPFHPF--HPFPALPENEGSGVGEQ---DGGLIGAEKVIN 576
Qy      576 -TTRPGSGLTNIKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGG 634
      : : :| : : |:| | | : : | | : |:| |:|
Db      577 SKNKVDENMVIDETLDVKEMIFNAE--RVGGLEERESVGPLREDFSLSSSALIGLLVIA 634
Qy      635 VVIATVIVITLVMLKKKQYTSIIHGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQ 694
      | | | | | |:| |:| |:| |:| |:| |:| |:| |:| |:| |:|
Db      635 VAIATVIVISLVMLRKRQYGTISHGIVEVDPMLTPEERHLNKMQNHYENPTYKYLEQMQ 694

```

Search completed: July 26, 2004, 12:46:33  
Job time : 38.3333 secs

OM protein - protein search, using sw model

Run on: July 26, 2004, 12:39:28 ; Search time 9 Seconds  
 (without alignments)  
 4032.544 Million cell updates/sec

Title: US-09-806-194A-16  
 Perfect score: 3651  
 Sequence: 1 MLPGLALLLLAAWTARALEV.....QQNGYENPTYKFFEQMQNKK 697

Scoring table: BLOSUM62  
 Gapop 10.0 , Gapext 0.5

Searched: 141681 seqs, 52070155 residues

Total number of hits satisfying chosen parameters: 141681

Minimum DB seq length: 0  
 Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
 Maximum Match 100%  
 Listing first 45 summaries

Database : SwissProt\_42:\*

Pred. No. is the number of results predicted by chance to have a  
 score greater than or equal to the score of the result being printed,  
 and is derived by analysis of the total score distribution.

# SUMMARIES

Result No.	Score	% Query		DB	ID	Description
		Match	Length			
1	3590.5	98.3	770	1	A4_HUMAN	P05067 h amyloid b
2	3590.5	98.3	770	1	A4_MACFA	P53601 m amyloid b
3	3584	98.2	751	1	A4_SAISC	Q95241 s amyloid b
4	3535.5	96.8	770	1	A4_PIG	P79307 s amyloid b
5	3522.5	96.5	770	1	A4_CAVPO	Q60495 c amyloid b
6	3493.5	95.7	770	1	A4_MOUSE	P12023 m amyloid b
7	3493.5	95.7	770	1	A4_RAT	P08592 r amyloid b
8	2573	70.5	780	1	A4_TETFL	O73683 tetraodon f
9	2448.5	67.1	737	1	A4_FUGRU	O93279 fugu rubrip
10	1735	47.5	695	1	APP2_MOUSE	Q06335 mus musculu
11	1728	47.3	763	1	APP2_HUMAN	Q06481 homo sapien
12	1716	47.0	765	1	APP2_RAT	P15943 rattus norv
13	1190	32.6	650	1	APP1_HUMAN	P51693 homo sapien
14	1185	32.5	653	1	APP1_MOUSE	Q03157 mus musculu
15	817.5	22.4	686	1	A4_CAEL	Q10651 caenorhabdi
16	748.5	20.5	887	1	A4_DROME	P14599 drosophila
17	292	8.0	59	1	A4_BOVIN	Q28053 bos taurus

18	288	7.9	58	1	A4_RABIT	Q28748	oryctolagus
19	288	7.9	58	1	A4_SHEEP	Q28757	ovis aries
20	287	7.9	58	1	A4_CANFA	Q28280	canis famil
21	283	7.8	57	1	A4_URSMA	Q29149	ursus marit
22	185.5	5.1	407	1	IF68_HSVSA	Q01042	herpesvirus
23	185.5	5.1	993	1	SCP1_MOUSE	Q62209	mus musculu
24	176	4.8	2004	1	MYS3_HUMAN	Q92794	homo sapien
25	175.5	4.8	802	1	NAB3_YEAST	P38996	saccharomyc
26	173.5	4.8	793	1	CALD_HUMAN	Q05682	homo sapien
27	172	4.7	771	1	CALD_CHICK	P12957	gallus gall
28	172	4.7	1498	1	GOA3_HUMAN	Q08378	homo sapien
29	169.5	4.6	297	1	TRT2_HUMAN	P45379	homo sapien
30	169.5	4.6	721	1	YCF2_OENPI	P31568	oenothera p
31	168.5	4.6	1875	1	MLP1_YEAST	Q02455	saccharomyc
32	168	4.6	1240	1	YNJ1_YEAST	P53935	saccharomyc
33	167.5	4.6	1976	1	MYHA_HUMAN	P35580	homo sapien
34	166.5	4.6	816	1	YG3A_YEAST	P53278	saccharomyc
35	166.5	4.6	1976	1	MYHA_RAT	Q9jlt0	rattus norv
36	164.5	4.5	1447	1	GOA3_MOUSE	P55937	mus musculu
37	163.5	4.5	681	1	MP10_HUMAN	O00566	homo sapien
38	163	4.5	2017	1	MYSN_DROME	Q99323	drosophila
39	162.5	4.5	712	1	NUCL_RAT	P13383	rattus norv
40	160.5	4.4	1976	1	MYHA_BOVIN	Q27991	bos taurus
41	160	4.4	694	1	NUCL_CHICK	P15771	gallus gall
42	159.5	4.4	1955	1	PUMA_PARUN	O61308	parascaris
43	158	4.3	301	1	TRT2_CHICK	P02642	gallus gall
44	157.5	4.3	706	1	NUCL_HUMAN	P19338	homo sapien
45	156.5	4.3	1332	1	SPT7_YEAST	P35177	saccharomyc

# ALIGNMENTS

## RESULT 1

### A4\_HUMAN

ID A4\_HUMAN STANDARD; PRT; 770 AA.

AC P05067; P09000; P78438; Q13764; Q13778; Q13793; Q16011; Q16014;

AC Q16019; Q16020; Q9BT38; Q9UCA9; Q9UCB6; Q9UCC8; Q9UCD1; Q9UQ58;

DT 13-AUG-1987 (Rel. 05, Created)

DT 01-NOV-1991 (Rel. 20, Last sequence update)

DT 15-MAR-2004 (Rel. 43, Last annotation update)

DE Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease

DE amyloid protein) (Cerebral vascular amyloid peptide) (CVAP) (Protease

DE nexin-II) (PN-II) (APPI) (PreA4) [Contains: Soluble APP-alpha (S-APP-

DE alpha); Soluble APP-beta (S-APP-beta); C99; Beta-amyloid protein 42

DE (Beta-APP42); Beta-amyloid protein 40 (Beta-APP40); C83; P3(42);

DE P3(40); Gamma-CTF(59) (Gamma-secretase C-terminal fragment 59)

DE (Amyloid intracellular domain 59) (AID(59)); Gamma-CTF(57) (Gamma-

DE secretase C-terminal fragment 57) (Amyloid intracellular domain 57)

DE (AID(57)); Gamma-CTF(50) (Gamma-secretase C-terminal fragment 50)

DE (Amyloid intracellular domain 50) (AID(50)); C31].

GN APP OR A4 OR AD1.

OS Homo sapiens (Human).

OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

OC Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

OX NCBI\_TaxID=9606;

RN [1]

RP SEQUENCE FROM N.A. (ISOFORM APP695).  
 RC TISSUE=Brain;  
 RX MEDLINE=87144572; PubMed=2881207;  
 RA Kang J., Lemaire H.-G., Unterbeck A., Salbaum J.M., Masters C.L.,  
 RA Grzeschik K.-H., Multhaup G., Beyreuther K., Mueller-Hill B.;  
 RT "The precursor of Alzheimer's disease amyloid A4 protein resembles a  
 RT cell-surface receptor.";  
 RL Nature 325:733-736(1987).  
 RN [2]  
 RP SEQUENCE FROM N.A. (ISOFORM APP751).  
 RC TISSUE=Brain;  
 RX MEDLINE=88122639; PubMed=2893289;  
 RA Ponte P., Gonzalez-Dewhitt P., Schilling J., Miller J., Hsu D.,  
 RA Greenberg B., Davis K., Wallace W., Lieberburg I., Fuller F.,  
 RA Cordell B.;  
 RT "A new A4 amyloid mRNA contains a domain homologous to serine  
 RT proteinase inhibitors.";  
 RL Nature 331:525-527(1988).  
 RN [3]  
 RP SEQUENCE FROM N.A. (ISOFORM APP695).  
 RX MEDLINE=89128427; PubMed=2783775;  
 RA Lemaire H.-G., Salbaum J.M., Multhaup G., Kang J., Bayney R.M.,  
 RA Unterbeck A., Beyreuther K., Mueller-Hill B.;  
 RT "The PreA4(695) precursor protein of Alzheimer's disease A4 amyloid  
 RT is encoded by 16 exons.";  
 RL Nucleic Acids Res. 17:517-522(1989).  
 RN [4]  
 RP SEQUENCE FROM N.A. (ISOFORM APP770).  
 RX MEDLINE=90236318; PubMed=2110105;  
 RA Yoshikai S.-I., Sasaki H., Doh-Ura K., Furuya H., Sakaki Y.;  
 RT "Genomic organization of the human amyloid beta-protein precursor  
 RT gene.";  
 RL Gene 87:257-263(1990).  
 RN [5]  
 RP ERRATUM, AND REVISIONS.  
 RA Yoshikai S.-I., Sasaki H., Doh-ura K., Furuya H., Sakaki Y.;  
 RL Gene 102:291-292(1991).  
 RN [6]  
 RP SEQUENCE FROM N.A. (ISOFORM L-APP733).  
 RC TISSUE=Leukocyte;  
 RX MEDLINE=92268136; PubMed=1587857;  
 RA Koenig G., Moenning U., Czech C., Prior R., Banati R.,  
 RA Schreiter-Gasser U., Bauer J., Masters C.L., Beyreuther K.;  
 RT "Identification and differential expression of a novel alternative  
 RT splice isoform of the beta A4 amyloid precursor protein (APP) mRNA in  
 RT leukocytes and brain microglial cells.";  
 RL J. Biol. Chem. 267:10804-10809(1992).  
 RN [7]  
 RP SEQUENCE FROM N.A. (ISOFORM APP770).  
 RX MEDLINE=97263807; PubMed=9108164;  
 RA Hattori M., Tsukahara F., Furuhashi Y., Tanahashi H., Hirose M.,  
 RA Saito M., Tsukuni S., Sakaki Y.;  
 RT "A novel method for making nested deletions and its application for  
 RT sequencing of a 300 kb region of human APP locus.";  
 RL Nucleic Acids Res. 25:1802-1808(1997).  
 RN [8]  
 RP SEQUENCE FROM N.A. (ISOFORM APP639).

RC TISSUE=Brain;  
 RX MEDLINE=22744650; PubMed=12859342;  
 RA Tang K., Wang C., Shen C., Sheng S., Ravid R., Jing N.;  
 RT "Identification of a novel alternative splicing isoform of human  
 RT amyloid precursor protein gene, APP639.";  
 RL Eur. J. Neurosci. 18:102-108(2003).  
 RN [9]  
 RP SEQUENCE FROM N.A. (ISOFORM APP305).  
 RC TISSUE=Pancreas;  
 RX MEDLINE=22388257; PubMed=12477932;  
 RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,  
 RA Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,  
 RA Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,  
 RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,  
 RA Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,  
 RA Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,  
 RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,  
 RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,  
 RA Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,  
 RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,  
 RA Villalón D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,  
 RA Fahey J., Helton E., Kettelman M., Madan A., Rodrigues S., Sanchez A.,  
 RA Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,  
 RA Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,  
 RA Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,  
 RA Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,  
 RA Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;  
 RT "Generation and initial analysis of more than 15,000 full-length  
 RT human and mouse cDNA sequences.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).  
 RN [10]  
 RP SEQUENCE OF 1-10 FROM N.A.  
 RC TISSUE=Liver;  
 RX MEDLINE=89016647; PubMed=3140222;  
 RA Schon E.A., Mita S., Sadlock J., Herbert J.;  
 RT "A cDNA specifying the human amyloid beta precursor protein (ABPP)  
 RT encodes a 95-kDa polypeptide.";  
 RL Nucleic Acids Res. 16:9351-9351(1988).  
 RN [11]  
 RP ERRATUM, AND REVISIONS.  
 RA Mita S., Sadlock J., Herbert J., Schon E.A.;  
 RL Nucleic Acids Res. 16:11402-11402(1988).  
 RN [12]  
 RP SEQUENCE OF 1-75 FROM N.A.  
 RX MEDLINE=89165870; PubMed=2538123;  
 RA La Fauci G., Lahiri D.K., Salton S.R., Robakis N.K.;  
 RT "Characterization of the 5'-end region and the first two exons of the  
 RT beta-protein precursor gene.";  
 RL Biochem. Biophys. Res. Commun. 159:297-304(1989).  
 RN [13]  
 RP SEQUENCE OF 18-50.  
 RC TISSUE=Fibroblast;  
 RX MEDLINE=87250462; PubMed=3597385;  
 RA van Nostrand W.E., Cunningham D.D.;  
 RT "Purification of protease nexin II from human fibroblasts.";  
 RL J. Biol. Chem. 262:8508-8514(1987).  
 RN [14]



RP PARTIAL SEQUENCE FROM N.A. (ISOFORM APP751).  
 RC TISSUE=Brain;  
 RX MEDLINE=89346754; PubMed=2569763;  
 RA de Sauvage F., Octave J.N.;  
 RT "A novel mRNA of the A4 amyloid precursor gene coding for a possibly  
 RT secreted protein.";  
 RL Science 245:651-653(1989).  
 RN [15]  
 RP PARTIAL SEQUENCE FROM N.A. (ISOFORM APP695).  
 RC TISSUE=Brain;  
 RX MEDLINE=87231971; PubMed=3035574;  
 RA Robakis N.K., Ramakrishna N., Wolfe G., Wisniewski H.M.;  
 RT "Molecular cloning and characterization of a cDNA encoding the  
 RT cerebrovascular and the neuritic plaque amyloid peptides.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 84:4190-4194(1987).  
 RN [16]  
 RP SEQUENCE OF 286-366 FROM N.A.  
 RX MEDLINE=88122640; PubMed=2893290;  
 RA Tanzi R.E., McClatchey A.I., Lamperti E.D., Villa-Komaroff L.,  
 RA Gusella J.F., Neve R.L.;  
 RT "Protease inhibitor domain encoded by an amyloid protein precursor  
 RT mRNA associated with Alzheimer's disease.";  
 RL Nature 331:528-530(1988).  
 RN [17]  
 RP SEQUENCE OF 287-367 FROM N.A.  
 RX MEDLINE=88122641; PubMed=2893291;  
 RA Kitaguchi N., Takahashi Y., Tokushima Y., Shiojiri S., Ito H.;  
 RT "Novel precursor of Alzheimer's disease amyloid protein shows  
 RT protease inhibitory activity.";  
 RL Nature 331:530-532(1988).  
 RN [18]  
 RP SEQUENCE OF 507-770 FROM N.A.  
 RC TISSUE=Brain cortex;  
 RX MEDLINE=88124954; PubMed=2893379;  
 RA Zain S.B., Salim M., Chou W.G., Sajdel-Sulkowska E.M., Majocha R.E.,  
 RA Marotta C.A.;  
 RT "Molecular cloning of amyloid cDNA derived from mRNA of the Alzheimer  
 RT disease brain: coding and noncoding regions of the fetal precursor  
 RT mRNA are expressed in the cortex.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 85:929-933(1988).  
 RN [19]  
 RP SEQUENCE OF 523-555, AND COLLAGEN-BINDING DOMAIN.  
 RX MEDLINE=96139497; PubMed=8576160;  
 RA Beher D., Hesse L., Masters C.L., Multhaup G.;  
 RT "Regulation of amyloid protein precursor (APP) binding to collagen and  
 RT mapping of the binding sites on APP and collagen type I.";  
 RL J. Biol. Chem. 271:1613-1620(1996).  
 RN [20]  
 RP SEQUENCE OF 655-737 FROM N.A., AND VARIANTS AD PHE-717; AD ILE-717  
 RP AND AD GLY-717.  
 RX MEDLINE=93236601; PubMed=8476439;  
 RA Denman R.B., Rosenzwaig R., Miller D.L.;  
 RT "A system for studying the effect(s) of familial Alzheimer disease  
 RT mutations on the processing of the beta-amyloid peptide precursor.";  
 RL Biochem. Biophys. Res. Commun. 192:96-103(1993).  
 RN [21]  
 RP SEQUENCE OF 656-737 FROM N.A.



```

Db      661 IKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVIATVIVITL 720
Qy      646 VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
Db      721 VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 770

```

# RESULT 2

## A4\_MACFA

```

ID      A4_MACFA          STANDARD;          PRT;    770 AA.
AC      P53601; Q95KN7;
DT      01-OCT-1996 (Rel. 34, Created)
DT      28-FEB-2003 (Rel. 41, Last sequence update)
DT      28-FEB-2003 (Rel. 41, Last annotation update)
DE      Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease
DE      amyloid protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha);
DE      Soluble APP-beta (S-APP-beta); C99; Beta-amyloid protein 42 (Beta-
DE      APP42); Beta-amyloid protein 40 (Beta-APP40); C83; P3(42); P3(40);
DE      Gamma-CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-CTF(57)
DE      (Gamma-secretase C-terminal fragment 57); Gamma-CTF(50) (Gamma-
DE      secretase C-terminal fragment 50); C31].
GN      APP.
OS      Macaca fascicularis (Crab eating macaque) (Cynomolgus monkey).
OC      Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC      Mammalia; Eutheria; Primates; Catarrhini; Cercopithecidae;
OC      Cercopithecinae; Macaca.
OX      NCBI_TaxID=9541;
RN      [1]
RP      SEQUENCE FROM N.A. (ISOFORMS APP695 AND APP770).
RC      TISSUE=Cerebellum;
RX      MEDLINE=91273117; PubMed=1905108;
RA      Podlisny M.B., Tolan D.R., Selkoe D.J.;
RT      "Homology of the amyloid beta protein precursor in monkey and human
RT      supports a primate model for beta amyloidosis in Alzheimer's
RT      disease.";
RL      Am. J. Pathol. 138:1423-1435(1991).
CC      -!- FUNCTION: Functions as a cell surface receptor and performs
CC      physiological functions on the surface of neurons relevant to
CC      neurite growth, neuronal adhesion and axonogenesis. Involved in
CC      cell mobility and transcription regulation through protein-protein
CC      interactions (By similarity). Can promote transcription activation
CC      through binding to APBB1/Tip60 and inhibit Notch signaling through
CC      interaction with Numb (By similarity). Couples to apoptosis-
CC      inducing pathways such as those mediated by G(0) and JIP (By
CC      similarity). Inhibits G(0) alpha ATPase activity (By similarity).
CC      Acts as a kinesin I membrane receptor, mediating the axonal
CC      transport of beta-secretase and presenilin 1 (By similarity). May
CC      be involved in copper homeostasis/oxidative stress through copper
CC      ion reduction. In vitro, copper-metallated APP induces neuronal
CC      death directly or is potentiated through Cu(II)-mediated low-
CC      density lipoprotein oxidation (By similarity). Can regulate
CC      neurite outgrowth through binding to components of the
CC      extracellular matrix such as heparin and collagen I and IV (By
CC      similarity). The splice isoforms that contain the BPTI domain
CC      possess protease inhibitor activity (By similarity).
CC      -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators

```

CC with metal-reducing activity. Bind transient metals such as  
 CC copper, zinc and iron (By similarity).  
 CC -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved  
 CC peptides, including C31, are potent enhancers of neuronal  
 CC apoptosis (By similarity).  
 CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several  
 CC cytoplasmic proteins, including APBB family members, the APBA  
 CC family, MAPK8IP1, and SHC1, Numb and Dab1 (By similarity). Binding  
 CC to Dab1 inhibits its serine phosphorylation (By similarity). Also  
 CC interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2  
 CC (via its TPR domains) (By similarity), APPBP2 (via BaSS) and DDB1.  
 CC In vitro, it binds MAPT via the MT-binding domains (By  
 CC similarity). Associates with microtubules in the presence of ATP  
 CC and in a kinesin-dependent manner (By similarity).  
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface  
 CC protein that rapidly becomes internalized via clathrin-coated  
 CC pits. During maturation, the immature APP (N-glycosylated in the  
 CC endoplasmic reticulum) moves to the Golgi complex where complete  
 CC maturation occurs (O-glycosylated and sulfated). After alpha-  
 CC secretase cleavage, soluble APP is released into the extracellular  
 CC space and the C-terminal is internalized to endosomes and  
 CC lysosomes. Some APP accumulates in secretory transport vesicles  
 CC leaving the late Golgi compartment and returns to the cell  
 CC surface. Gamma-CTF(59) peptide is located to both the cytoplasm  
 CC and nuclei of neurons (By similarity).  
 CC -!- ALTERNATIVE PRODUCTS:  
 CC Event=Alternative splicing; Named isoforms=2;  
 CC Comment=Additional isoforms seem to exist;  
 CC Name=APP770;  
 CC IsoId=P53601-1; Sequence=Displayed;  
 CC Name=APP695;  
 CC IsoId=P53601-2; Sequence=VSP\_000010, VSP\_000011;  
 CC -!- DOMAIN: The basolateral sorting signal (BaSS) is required for  
 CC sorting of membrane proteins to the basolateral surface of  
 CC epithelial cells (By similarity).  
 CC -!- DOMAIN: The NPXY sequence motif found in many tyrosine-  
 CC phosphorylated proteins is required for the specific binding of  
 CC the PID domain. However additional amino acids either N- or C-  
 CC terminal to the NPXY motif are often required for complete  
 CC interaction. The PID domain-containing proteins which bind APP  
 CC require the YENPTY motif for full interaction. These interactions  
 CC are independent of phosphorylation on the terminal tyrosine  
 CC residue. The NPXY site is also involved in clathrin-mediated  
 CC endocytosis (By similarity).  
 CC -!- PTM: Proteolytically processed under normal cellular conditions.  
 CC Cleavage by alpha-secretase or alternatively by beta-secretase  
 CC leads to generation and extracellular release of soluble APP  
 CC peptides, S-APP-alpha and S-APP-beta, respectively, and the  
 CC retention of corresponding membrane-anchored C-terminal fragments,  
 CC C83 and C99. Subsequent processing of C83 by gamma-secretase  
 CC yields P3 peptides. This is the major secretory pathway and is  
 CC nonamyloidogenic. Alternatively, presenilin/nicastrin-mediated  
 CC gamma-secretase processing of C99 releases the amyloid beta  
 CC proteins, amyloid-beta 40 (Abeta40) and amyloid-beta 42 (Abeta42),  
 CC major components of amyloid plaques, and the cytotoxic C-terminal  
 CC fragments, gamma-CTF(50), gamma-CTF(57) and gamma-CTF(59) (By  
 CC similarity).

CC -!- PTM: Proteolytically cleaved by caspases during neuronal apoptosis  
 CC (By similarity). Cleavage at Asp-739 by either caspase-3, -8 or -9  
 CC results in the production of the neurotoxic C31 peptide and the  
 CC increased production of beta-amyloid peptides (By similarity).  
 CC -!- PTM: N- and O-glycosylated (By similarity).  
 CC -!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and  
 CC serine residues is neuron-specific. Phosphorylation can affect APP  
 CC processing, neuronal differentiation and interaction with other  
 CC proteins (By similarity).  
 CC -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and  
 CC zinc, can induce histidine-bridging between beta-amyloid molecules  
 CC resulting in beta-amyloid-metal aggregates (By similarity).  
 CC Extracellular zinc-binding increases binding of heparin to APP and  
 CC inhibits collagen-binding (By similarity).  
 CC -!- SIMILARITY: Belongs to the APP family.  
 CC -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.

CC -----  
 CC This SWISS-PROT entry is copyright. It is produced through a collaboration  
 CC between the Swiss Institute of Bioinformatics and the EMBL outstation -  
 CC the European Bioinformatics Institute. There are no restrictions on its  
 CC use by non-profit institutions as long as its content is in no way  
 CC modified and this statement is not removed. Usage by and for commercial  
 CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>  
 CC or send an email to [license@isb-sib.ch](mailto:license@isb-sib.ch)).  
 CC -----

DR EMBL; M58727; AAA36829.1; -.  
 DR EMBL; M58726; AAA36828.1; -.  
 DR HSSP; P05067; 1AAP.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR InterPro; IPR002223; Kunitz\_BPTI.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR Pfam; PF00014; Kunitz\_BPTI; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR PRINTS; PR00759; BASICPTASE.  
 DR ProDom; PD000222; Kunitz\_BPTI; 1.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR SMART; SM00131; KU; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 DR PROSITE; PS00280; BPTI\_KUNITZ\_1; 1.  
 DR PROSITE; PS50279; BPTI\_KUNITZ\_2; 1.  
 KW Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;  
 KW Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;  
 KW Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;  
 KW Proteoglycan; Alternative splicing; Amyloid.  
 FT SIGNAL 1 17 BY SIMILARITY.  
 FT CHAIN 18 770 AMYLOID BETA A4 PROTEIN.  
 FT CHAIN 18 687 SOLUBLE APP-ALPHA (POTENTIAL).  
 FT CHAIN 18 671 SOLUBLE APP-BETA (POTENTIAL).  
 FT CHAIN 672 770 C99 (POTENTIAL).  
 FT CHAIN 672 713 BETA-AMYLOID PROTEIN 42 (POTENTIAL).  
 FT CHAIN 672 711 BETA-AMYLOID PROTEIN 40 (POTENTIAL).  
 FT CHAIN 688 770 C83 (POTENTIAL).  
 FT CHAIN 688 713 P3(42) (POTENTIAL).

FT	CHAIN	688	711	P3(40) (POTENTIAL).
FT	CHAIN	712	770	GAMMA-CTF(59) (POTENTIAL).
FT	CHAIN	714	770	GAMMA-CTF(57) (POTENTIAL).
FT	CHAIN	721	770	GAMMA-CTF(50) (POTENTIAL).
FT	CHAIN	740	770	C31 (POTENTIAL).
FT	DOMAIN	18	699	EXTRACELLULAR (POTENTIAL).
FT	TRANSMEM	700	723	POTENTIAL.
FT	DOMAIN	724	770	CYTOPLASMIC (POTENTIAL).
FT	DOMAIN	96	110	HEPARIN-BINDING (BY SIMILARITY).
FT	DOMAIN	181	188	ZINC-BINDING (BY SIMILARITY).
FT	DOMAIN	291	341	BPTI/KUNITZ INHIBITOR.
FT	DOMAIN	391	423	HEPARIN-BINDING (BY SIMILARITY).
FT	DOMAIN	491	522	HEPARIN-BINDING (BY SIMILARITY).
FT	DOMAIN	523	540	COLLAGEN-BINDING (BY SIMILARITY).
FT	DOMAIN	732	751	INTERACTION WITH G(O)-ALPHA
FT				(BY SIMILARITY).
FT	DOMAIN	230	260	ASP/GLU-RICH (ACIDIC).
FT	DOMAIN	274	280	POLY-THR.
FT	SITE	144	144	REQUIRED FOR COPPER(II) REDUCTION
FT				(BY SIMILARITY).
FT	ACT_SITE	301	302	REACTIVE BOND (BY SIMILARITY).
FT	SITE	671	672	CLEAVAGE (BY BETA-SECRETASE)
FT				(BY SIMILARITY).
FT	SITE	672	673	CLEAVAGE (BY CASPASE-6) (BY SIMILARITY).
FT	SITE	687	688	CLEAVAGE (BY ALPHA-SECRETASE)
FT				(BY SIMILARITY).
FT	SITE	704	704	IMPLICATED IN FREE RADICAL PROPAGATION
FT				(BY SIMILARITY).
FT	SITE	706	706	INVOLVED IN OXIDATIVE REACTIONS
FT				(BY SIMILARITY).
FT	SITE	711	712	CLEAVAGE (BY GAMMA-SECRETASE; SITE 1)
FT				(BY SIMILARITY).
FT	SITE	713	714	CLEAVAGE (BY GAMMA-SECRETASE; SITE 2)
FT				(BY SIMILARITY).
FT	SITE	720	721	CLEAVAGE (BY GAMMA-SECRETASE; SITE 3)
FT				(BY SIMILARITY).
FT	SITE	724	734	BASOLATERAL SORTING SIGNAL
FT				(BY SIMILARITY).
FT	SITE	739	740	CLEAVAGE (BY CASPASES-3,-6,-8 OR -9)

Query Match 98.3%; Score 3590.5; DB 1; Length 770;  
 Best Local Similarity 90.1%; Pred. No. 9.8e-169;  
 Matches 694; Conservative 1; Mismatches 0; Indels 75; Gaps 1;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240

Db	181		GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEE	240
Qy	241		EADDEDEDEDEGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVR-----	288
Db	241		EADDEDEDEDEGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVREVCSEQAETGPC	300
Qy	289		-----	288
Db	301		RAMISRWFYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMVCGSVMSQSLRKTTRREPLTRD	360
Qy	289		---VPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQA	345
Db	361	:	PVKLP'TTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQA	420
Qy	346		KNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITAL	405
Db	421		KNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITAL	480
Qy	406		QAVPPRPRHVFENMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER	465
Db	481		QAVPPRPRHVFENMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER	540
Qy	466		MNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDDLANMISEPRISYGNDAIMPSTET	525
Db	541		MNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDDLANMISEPRISYGNDAIMPSTET	600
Qy	526		KTTVELLPVNGEFSLDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTN	585
Db	601		KTTVELLPVNGEFSLDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTN	660
Qy	586		IKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITL	645
Db	661		IKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITL	720
Qy	646		VMLKKKQYTSIHGHGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	695
Db	721		VMLKKKQYTSIHGHGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	770

RESULT 3

A4\_SAISC

ID A4\_SAISC STANDARD; PRT; 751 AA.

AC Q95241;

DT 15-DEC-1998 (Rel. 37, Created)

DT 15-DEC-1998 (Rel. 37, Last sequence update)

DT 10-OCT-2003 (Rel. 42, Last annotation update)

DE Amyloid beta A4 protein precursor (APP) (Alzheimer's disease amyloid  
 DE protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha); Soluble  
 DE APP-beta (S-APP-beta); C99; Beta-amyloid protein 42 (Beta-APP42);  
 DE Beta-amyloid protein 40 (Beta-APP40); C83; P3(42); P3(40); Gamma-  
 DE CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-CTF(57)  
 DE (Gamma-secretase C-terminal fragment 57); Gamma-CTF(50) (Gamma-  
 DE secretase C-terminal fragment 50); C31].

GN APP.

OS Saimiri sciureus (Common squirrel monkey).

OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

OC Mammalia; Eutheria; Primates; Platyrrhini; Cebidae; Cebinae; Saimiri.  
 OX NCBI\_TaxID=9521;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RC TISSUE=Kidney, and Liver;  
 RX MEDLINE=96108492; PubMed=8532114;  
 RA Levy E., Amorim A., Frangione B., Walker L.C.;  
 RT "Beta-amyloid precursor protein gene in squirrel monkeys with  
 RT cerebral amyloid angiopathy."  
 RL Neurobiol. Aging 16:805-808(1995).  
 CC -!- FUNCTION: Functions as a cell surface receptor and performs  
 CC physiological functions on the surface of neurons relevant to  
 CC neurite growth, neuronal adhesion and axonogenesis. Involved in  
 CC cell mobility and transcription regulation through protein-protein  
 CC interactions (By similarity). Can promote transcription activation  
 CC through binding to APBB1/Tip60 and inhibit Notch signaling through  
 CC interaction with Numb (By similarity). Couples to apoptosis-  
 CC inducing pathways such as those mediated by G(O) and JIP (By  
 CC similarity). Inhibits G(O) alpha ATPase activity (By similarity).  
 CC Acts as a kinesin I membrane receptor, mediating the axonal  
 CC transport of beta-secretase and presenilin 1 (By similarity). May  
 CC be involved in copper homeostasis/oxidative stress through copper  
 CC ion reduction. In vitro, copper-metallated APP induces neuronal  
 CC death directly or is potentiated through Cu(II)-mediated low-  
 CC density lipoprotein oxidation (By similarity). Can regulate  
 CC neurite outgrowth through binding to components of the  
 CC extracellular matrix such as heparin and collagen I and IV (By  
 CC similarity). The splice isoforms that contain the BPTI domain  
 CC possess protease inhibitor activity (By similarity).  
 CC -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators  
 CC with metal-reducing activity. Bind transient metals such as  
 CC copper, zinc and iron (By similarity).  
 CC -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved  
 CC peptides, including C31, are potent enhancers of neuronal  
 CC apoptosis (By similarity).  
 CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several  
 CC cytoplasmic proteins, including APBB family members, the APBA  
 CC family, MAPK8IP1, and SHC1, Numb and Dab1 (By similarity). Binding  
 CC to Dab1 inhibits its serine phosphorylation (By similarity). Also  
 CC interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2  
 CC (via its TPR domains) (By similarity), APPBP2 (via BaSS) and DDB1.  
 CC In vitro, it binds MAPT via the MT-binding domains (By  
 CC similarity). Associates with microtubules in the presence of ATP  
 CC and in a kinesin-dependent manner (By similarity).  
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface  
 CC protein that rapidly becomes internalized via clathrin-coated  
 CC pits. During maturation, the immature APP (N-glycosylated in the  
 CC endoplasmic reticulum) moves to the Golgi complex where complete  
 CC maturation occurs (O-glycosylated and sulfated). After alpha-  
 CC secretase cleavage, soluble APP is released into the extracellular  
 CC space and the C-terminal is internalized to endosomes and  
 CC lysosomes. Some APP accumulates in secretory transport vesicles  
 CC leaving the late Golgi compartment and returns to the cell  
 CC surface. Gamma-CTF(59) peptide is located to both the cytoplasm  
 CC and nuclei of neurons (By similarity).  
 CC -!- ALTERNATIVE PRODUCTS:  
 CC Event=Alternative splicing; Named isoforms=2;



```

CC      Comment=Additional isoforms seem to exist;
CC      Name=APP770;
CC      IsoId=Q95241-1; Sequence=Displayed;
CC      Name=APP695;
CC      IsoId=Q95241-2; Sequence=Not described;
CC      -!- DOMAIN: The basolateral sorting signal (BaSS) is required for
CC      sorting of membrane proteins to the basolateral surface of
CC      epithelial cells (By similarity).
CC      -!- DOMAIN: The NPXY sequence motif found in many tyrosine-
CC      phosphorylated proteins is required for the specific binding of
CC      the PID domain. However additional amino acids either N- or C-
CC      terminal to the NPXY motif are often required for complete
CC      interaction. The PID domain-containing proteins which bind APP
CC      require the YENPTY motif for full interaction. These interactions
CC      are independent of phosphorylation on the terminal tyrosine
CC      residue. The NPXY site is also involved in clathrin-mediated
CC      endocytosis (By similarity).
CC      -!- PTM: Proteolytically processed under normal cellular conditions.
CC      Cleavage by alpha-secretase or alternatively by beta-secretase
CC      leads to generation and extracellular release of soluble APP
CC      peptides, S-APP-alpha and S-APP-beta, respectively, and the
CC      retention of corresponding membrane-anchored C-terminal fragments,
CC      C83 and C99. Subsequent processing of C83 by gamma-secretase
CC      yields P3 peptides. This is the major secretory pathway and is
CC      nonamyloidogenic. Alternatively, presenilin/nicastrin-mediated
CC      gamma-secretase processing of C99 releases the amyloid beta
CC      proteins, amyloid-beta 40 (Abeta40) and amyloid-beta 42 (Abeta42),
CC      major components of amyloid plaques, and the cytotoxic C-terminal
CC      fragments, gamma-CTF(50), gamma-CTF(57) and gamma-CTF(59) (By
CC      similarity).
CC      -!- PTM: Proteolytically cleaved by caspases during neuronal apoptosis
CC      (By similarity). Cleavage at Asp-720 by either caspase-3, -8 or -9
CC      results in the production of the neurotoxic C31 peptide and the
CC      increased production of beta-amyloid peptides (By similarity).
CC      -!- PTM: N- and O-glycosylated (By similarity).
CC      -!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and
CC      serine residues is neuron-specific. Phosphorylation can affect APP
CC      processing, neuronal differentiation and interaction with other
CC      proteins (By similarity).
CC      -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and
CC      zinc, can induce histidine-bridging between beta-amyloid molecules
CC      resulting in beta-amyloid-metal aggregates (By similarity).
CC      Extracellular zinc-binding increases binding of heparin to APP and
CC      inhibits collagen-binding (By similarity).
CC      -!- SIMILARITY: Belongs to the APP family.
CC      -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.
CC      -----
CC      This SWISS-PROT entry is copyright. It is produced through a collaboration
CC      between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC      the European Bioinformatics Institute. There are no restrictions on its
CC      use by non-profit institutions as long as its content is in no way
CC      modified and this statement is not removed. Usage by and for commercial
CC      entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC      or send an email to license@isb-sib.ch).
CC      -----
DR      EMBL; S81024; AAD14347.1; -.
DR      HSSP; P05067; 1AAP.

```

DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR InterPro; IPR002223; Kunitz\_BPTI.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR Pfam; PF00014; Kunitz\_BPTI; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR PRINTS; PR00759; BASICPTASE.  
 DR ProDom; PD000222; Kunitz\_BPTI; 1.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR SMART; SM00131; KU; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 DR PROSITE; PS00280; BPTI\_KUNITZ\_1; 1.  
 DR PROSITE; PS50279; BPTI\_KUNITZ\_2; 1.  
 KW Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;  
 KW Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;  
 KW Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;  
 KW Proteoglycan; Amyloid; Alternative splicing.  
 FT SIGNAL 1 17 BY SIMILARITY.  
 FT CHAIN 18 751 A4 PROTEIN.  
 FT CHAIN 18 668 SOLUBLE APP-ALPHA (POTENTIAL).  
 FT CHAIN 18 652 SOLUBLE APP-BETA (POTENTIAL).  
 FT CHAIN 653 751 C99 (POTENTIAL).  
 FT CHAIN 653 694 BETA-AMYLOID PROTEIN 42 (POTENTIAL).  
 FT CHAIN 653 692 BETA-AMYLOID PROTEIN 40 (POTENTIAL).  
 FT CHAIN 669 751 C83 (POTENTIAL).  
 FT CHAIN 669 694 P3(42) (POTENTIAL).  
 FT CHAIN 669 692 P3(40) (POTENTIAL).  
 FT CHAIN 693 751 GAMMA-CTF(59) (POTENTIAL).  
 FT CHAIN 695 751 GAMMA-CTF(57) (POTENTIAL).  
 FT CHAIN 702 751 GAMMA-CTF(50) (POTENTIAL).  
 FT CHAIN 721 751 C31 (POTENTIAL).  
 FT DOMAIN 18 680 EXTRACELLULAR (POTENTIAL).  
 FT TRANSMEM 681 704 POTENTIAL.  
 FT DOMAIN 705 751 CYTOPLASMIC (POTENTIAL).  
 FT DOMAIN 96 110 HEPARIN-BINDING (BY SIMILARITY).  
 FT DOMAIN 181 188 ZINC-BINDING (BY SIMILARITY).  
 FT DOMAIN 291 341 BPTI/KUNITZ INHIBITOR.  
 FT DOMAIN 316 344 HEPARIN-BINDING (BY SIMILARITY).  
 FT DOMAIN 363 428 HEPARIN-BINDING (BY SIMILARITY).  
 FT DOMAIN 504 521 COLLAGEN-BINDING (BY SIMILARITY).  
 FT DOMAIN 713 732 INTERACTION WITH G(O)-ALPHA  
 FT (BY SIMILARITY).  
 FT DOMAIN 230 260 ASP/GLU-RICH (ACIDIC).  
 FT DOMAIN 274 280 POLY-THR.  
 FT SITE 144 144 REQUIRED FOR COPPER(II) REDUCTION  
 FT (BY SIMILARITY).  
 FT ACT\_SITE 301 302 REACTIVE BOND.  
 FT SITE 652 653 CLEAVAGE (BY BETA-SECRETASE)  
 FT (BY SIMILARITY).  
 FT SITE 653 654 CLEAVAGE (BY CASPASE-6) (BY SIMILARITY).  
 FT SITE 668 669 CLEAVAGE (BY ALPHA-SECRETASE)  
 FT (BY SIMILARITY).  
 FT SITE 685 685 INVOLVED IN FREE RADICAL PROPAGATION  
 FT (BY SIMILARITY).



```

Db      541 DEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSLDDLQ 600
Qy      545 PWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEFRHDS 604
        |||
Db      601 PWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEFRHDS 660
Qy      605 GYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIH HG VVEVD 664
        |||
Db      661 GYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIH HG VVEVD 720
Qy      665 AAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
        |||
Db      721 AAVTPEERHLSKMQQNGYENPTYKFFEQMQN 751

```

#### RESULT 4

##### A4\_PIG

```

ID_ A4_PIG          STANDARD;          PRT;    770 AA.
AC  P79307; Q29023; Q9TUI0;
DT  01-NOV-1997 (Rel. 35, Created)
DT  10-OCT-2003 (Rel. 42, Last sequence update)
DT  10-OCT-2003 (Rel. 42, Last annotation update)
DE  Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease
DE  amyloid protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha);
DE  Soluble APP-beta (S-APP-beta); C99; Beta-amyloid protein 42 (Beta-
DE  APP42); Beta-amyloid protein 40 (Beta-APP40); C83; P3(42); P3(40);
DE  Gamma-CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-CTF(57)
DE  (Gamma-secretase C-terminal fragment 57); Gamma-CTF(50) (Gamma-
DE  secretase C-terminal fragment 50); C31].
OS  Sus scrofa (Pig).
OC  Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC  Mammalia; Eutheria; Cetartiodactyla; Suina; Suidae; Sus.
OX  NCBI_TaxID=9823;
RN  [1]
RP  SEQUENCE FROM N.A.
RA  Kimura A., Takahashi T.;
RT  "Amyloid precursor protein 770.";
RL  Submitted (SEP-1999) to the EMBL/GenBank/DDBJ databases.
RN  [2]
RP  SEQUENCE OF 1-136 FROM N.A.
RC  TISSUE=Small intestine;
RA  Winteroe A.K., Fredholm M.;
RT  "Evaluation and characterization of a porcine small intestine cDNA
RT  library.";
RL  Submitted (JAN-1997) to the EMBL/GenBank/DDBJ databases.
RN  [3]
RP  SEQUENCE OF 667-723 FROM N.A.
RC  TISSUE=Brain;
RX  MEDLINE=92017079; PubMed=1656157;
RA  Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;
RT  "Conservation of the sequence of the Alzheimer's disease amyloid
RT  peptide in dog, polar bear and five other mammals by cross-species
RT  polymerase chain reaction analysis.";
RL  Brain Res. Mol. Brain Res. 10:299-305(1991).
CC  -!- FUNCTION: Functions as a cell surface receptor and performs
CC  physiological functions on the surface of neurons relevant to
CC  neurite growth, neuronal adhesion and axonogenesis. Involved in

```

cell mobility and transcription regulation through protein-protein interactions (By similarity). Can promote transcription activation through binding to APBB1/Tip60 and inhibit Notch signaling through interaction with Numb (By similarity). Couples to apoptosis-inducing pathways such as those mediated by G(0) and JIP (By similarity). Inhibits G(0) alpha ATPase activity (By similarity). Acts as a kinesin I membrane receptor, mediating the axonal transport of beta-secretase and presenilin 1 (By similarity). May be involved in copper homeostasis/oxidative stress through copper ion reduction (By similarity). In vitro, copper-metallated APP induces neuronal death directly or is potentiated through Cu(II)-mediated low-density lipoprotein oxidation (By similarity). Can regulate neurite outgrowth through binding to components of the extracellular matrix such as heparin and collagen I and IV (By similarity).

-!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators with metal-reducing activity. Bind transient metals such as copper, zinc and iron (By similarity).

-!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved peptides, including C31, are potent enhancers of neuronal apoptosis (By similarity).

-!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several cytoplasmic proteins, including APBB family members, the APBA family, MAPK8IP1, and SHC1, Numb and Dab1 (By similarity). Binding to Dab1 inhibits its serine phosphorylation (By similarity). Also interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2 (via its TPR domains) (By similarity), APPBP2 (via BaSS) and DDB1. In vitro, it binds MAPT via the MT-binding domains (By similarity). Associates with microtubules in the presence of ATP and in a kinesin-dependent manner (By similarity).

-!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface protein that rapidly becomes internalized via clathrin-coated pits. During maturation, the immature APP (N-glycosylated in the endoplasmic reticulum) moves to the Golgi complex where complete maturation occurs (O-glycosylated and sulfated). After alpha-secretase cleavage, soluble APP is released into the extracellular space and the C-terminal is internalized to endosomes and lysosomes. Some APP accumulates in secretory transport vesicles leaving the late Golgi compartment and returns to the cell surface. Gamma-CTF(59) peptide is located to both the cytoplasm and nuclei of neurons (By similarity).

-!- DOMAIN: The basolateral sorting signal (BaSS) is required for sorting of membrane proteins to the basolateral surface of epithelial cells (By similarity).

-!- DOMAIN: The NPXY sequence motif found in many tyrosine-phosphorylated proteins is required for the specific binding of the PID domain. However additional amino acids either N- or C-terminal to the NPXY motif are often required for complete interaction. The PID domain-containing proteins which bind APP require the YENPTY motif for full interaction. These interactions are independent of phosphorylation on the terminal tyrosine residue. The NPXY site is also involved in clathrin-mediated endocytosis (By similarity).

-!- PTM: Proteolytically processed under normal cellular conditions. Cleavage by alpha-secretase or alternatively by beta-secretase leads to generation and extracellular release of soluble APP peptides, S-APP-alpha and S-APP-beta, respectively, and the

retention of corresponding membrane-anchored C-terminal fragments, C83 and C99. Subsequent processing of C83 by gamma-secretase yields P3 peptides. This is the major secretory pathway and is nonamyloidogenic. Alternatively, presenilin/nicastrin-mediated gamma-secretase processing of C99 releases the amyloid beta proteins, amyloid-beta 40 (Abeta40) and amyloid-beta 42 (Abeta42), major components of amyloid plaques, and the cytotoxic C-terminal fragments, gamma-CTF(50), gamma-CTF(57) and gamma-CTF(59) (By similarity).

-!- PTM: Proteolytically cleaved by caspases during neuronal apoptosis (By similarity). Cleavage at Asp-739 by either caspase-3, -8 or -9 results in the production of the neurotoxic C31 peptide and the increased production of beta-amyloid peptides (By similarity).

-!- PTM: N- and O-glycosylated (By similarity).

-!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and serine residues is neuron-specific. Phosphorylation can affect APP processing, neuronal differentiation and interaction with other proteins (By similarity).

-!- PTM: Extracellular binding and reduction of copper, results in a corresponding oxidation of Cys-144 and Cys-158, and the formation of a disulfide bond (By similarity).

-!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and zinc, can induce histidine-bridging between beta-amyloid molecules resulting in beta-amyloid-metal aggregates (By similarity). Extracellular zinc-binding increases binding of heparin to APP and inhibits collagen-binding (By similarity).

-!- SIMILARITY: Belongs to the APP family.

-!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.

-----

This SWISS-PROT entry is copyright. It is produced through a collaboration between the Swiss Institute of Bioinformatics and the EMBL outstation - the European Bioinformatics Institute. There are no restrictions on its use by non-profit institutions as long as its content is in no way modified and this statement is not removed. Usage by and for commercial entities requires a license agreement (See <http://www.isb-sib.ch/announce/> or send an email to [license@isb-sib.ch](mailto:license@isb-sib.ch)).

-----

DR EMBL; AB032550; BAA84580.1; -.

DR EMBL; Z84022; CAB06313.1; -.

DR EMBL; X56127; CAA39592.1; -.

DR HSSP; P05067; 1AAP.

DR InterPro; IPR008155; A4\_APP.

DR InterPro; IPR008154; A4\_extra.

DR InterPro; IPR002223; Kunitz\_BPTI.

DR Pfam; PF02177; A4\_EXTRA; 1.

DR PRINTS; PR00203; AMYLOIDA4.

DR PRINTS; PR00759; BASICPTASE.

DR ProDom; PD000222; Kunitz\_BPTI; 1.

DR SMART; SM00006; A4\_EXTRA; 1.

DR SMART; SM00131; KU; 1.

DR PROSITE; PS00319; A4\_EXTRA; 1.

DR PROSITE; PS00320; A4\_INTRA; 1.

DR PROSITE; PS00280; BPTI\_KUNITZ\_1; 1.

DR PROSITE; PS50279; BPTI\_KUNITZ\_2; 1.

KW Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor; Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron; Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;

KW	Amyloid.			
FT	SIGNAL	1	17	BY SIMILARITY.
FT	CHAIN	18	770	AMYLOID BETA A4 PROTEIN.
FT	CHAIN	18	687	SOLUBLE APP-ALPHA (POTENTIAL).
FT	CHAIN	18	671	SOLUBLE APP-BETA (POTENTIAL).
FT	CHAIN	672	770	C99 (BY SIMILARITY).
FT	CHAIN	672	713	BETA-AMYLOID PROTEIN 42 (BY SIMILARITY).
FT	CHAIN	672	711	BETA-AMYLOID PROTEIN 40 (BY SIMILARITY).
FT	CHAIN	688	770	C83 (BY SIMILARITY).
FT	CHAIN	688	713	P3(42) (BY SIMILARITY).
FT	CHAIN	688	711	P3(40) (BY SIMILARITY).
FT	CHAIN	712	770	GAMMA-CTF(59).
FT	CHAIN	714	770	GAMMA-CTF(57).
FT	CHAIN	721	770	GAMMA-CTF(50) (BY SIMILARITY).
FT	CHAIN	740	770	C31 (DURING APOPTOSIS) (BY SIMILARITY).
FT	DOMAIN	18	699	EXTRACELLULAR (POTENTIAL).
FT	TRANSMEM	700	723	POTENTIAL.
FT	DOMAIN	724	770	CYTOPLASMIC (POTENTIAL).
FT	DOMAIN	96	110	HEPARIN-BINDING (BY SIMILARITY).
FT	DOMAIN	135	155	COPPER-BINDING (BY SIMILARITY).
FT	DOMAIN	181	188	ZINC-BINDING (BY SIMILARITY).
FT	DOMAIN	291	341	BPTI/KUNITZ INHIBITOR.
FT	DOMAIN	391	423	HEPARIN-BINDING (BY SIMILARITY).
FT	DOMAIN	491	522	HEPARIN-BINDING (BY SIMILARITY).
FT	DOMAIN	523	540	COLLAGEN-BINDING (BY SIMILARITY).
FT	DOMAIN	732	751	INTERACTION WITH G(O)-ALPHA (BY
FT				SIMILARITY).
FT	DOMAIN	230	260	ASP/GLU-RICH (ACIDIC).
FT	DOMAIN	274	280	POLY-THR.
FT	SITE	144	144	REQUIRED FOR COPPER(II) REDUCTION
FT				(BY SIMILARITY).
FT	ACT_SITE	301	302	REACTIVE BOND (BY SIMILARITY).
FT	SITE	671	672	CLEAVAGE (BY BETA-SECRETASE)
FT				(BY SIMILARITY).
FT	SITE	672	673	CLEAVAGE (BY CASPASE-6) (BY SIMILARITY).
FT	SITE	687	688	CLEAVAGE (BY ALPHA-SECRETASE)
FT				(BY SIMILARITY).
FT	SITE	704	704	IMPLICATED IN FREE RADICAL PROPAGATION
FT				(BY SIMILARITY).
FT	SITE	706	706	INVOLVED IN OXIDATIVE REACTIONS
FT				(BY SIMILARITY).
FT	SITE	711	712	CLEAVAGE (BY GAMMA-SECRETASE; SITE 1)
FT				(BY SIMILARITY).
FT	SITE	713	714	CLEAVAGE (BY GAMMA-SECRETASE; SITE 2)
FT				(BY SIMILARITY).
FT	SITE	720	721	CLEAVAGE (BY GAMMA-SECRETASE; SITE 3)

Query Match 96.8%; Score 3535.5; DB 1; Length 770;  
 Best Local Similarity 88.4%; Pred. No. 4.8e-166;  
 Matches 681; Conservative 8; Mismatches 6; Indels 75; Gaps 1;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
		:     :     :     :	
Db	1	MLPGLALVLLAAWTARALEVPTDGNAGLLAEPQVAMFCGKLNHMNMNVQNGKWEPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
		:     :     :     :	

```

Db      61 TCIGTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRSRKQCKTHTHIVIPYRCLVG 120
Qy      121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLP CGIDKFR 180
      |||
Db      121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLP CGIDKFR 180
Qy      181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240
      |||
Db      181 GVEFVCCPLAEESDNIDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVADVEEE 240
Qy      241 EADDDDEDEDGDEVEEEAEEPEYEEATERTTSIATTTTTTTTESVEEVVR----- 288
      |||
Db      241 EAEDDEDEDGDEVEEEAEEPEYEEATERTTSIATTTTTTTTESVEEVVREVCSEAETGPC 300
Qy      289 ----- 288
Db      301 RAMISRWFYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMVCGSVMSQSLLKTTQEHL PQD 360
Qy      289 ---VPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWE EAERQA 345
      :|||
Db      361 PVKLPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWE EAERQA 420
Qy      346 KNLPKADKKAVIQHFQEKVESLEQEAAANERQQLVETHMARVEAMLNDRRRRLALENYITAL 405
      |||
Db      421 KNLPKADKKAVIQHFQEKVESLEQEAAANERQQLVETHMARVEAMLNDRRRRLALENYITAL 480
Qy      406 QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER 465
      |||
Db      481 QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER 540
Qy      466 MNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDDLANMISEPRISYGN DALMPSLTET 525
      |||
Db      541 MNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDDLANMISEPRISYGN DALMPSLTET 600
Qy      526 KTTVELLPVNGEFSLDDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTN 585
      |||
Db      601 KTTVELLPVNGEFSLDDLQPWHPFGVDSVPANTENEVEPVDARPAADRGLTTRPGSGLTN 660
Qy      586 IKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITL 645
      |||
Db      661 IKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITL 720
Qy      646 VMLKKKQYTSIH HGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFE QMQN 695
      |||
Db      721 VMLKKKQYTSIH HGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFE QMQN 770

```

RESULT 5

A4\_CAVPO

ID A4\_CAVPO STANDARD; PRT; 770 AA.

AC Q60495; Q60496;

DT 10-OCT-2003 (Rel. 42, Created)

DT 10-OCT-2003 (Rel. 42, Last sequence update)

DT 10-OCT-2003 (Rel. 42, Last annotation update)

DE Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease

DE amyloid protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha);

DE Soluble APP-beta (S-APP-beta); CTF-alpha; CTF-beta; Beta-amyloid



DE protein 42 (Beta-APP42); Beta-amyloid protein 40 (Beta-APP40); P3(42);  
DE P3(40); CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-  
DE CTF(57) (Gamma-secretase C-terminal fragment 57); C31].  
GN APP.  
OS Cavia porcellus (Guinea pig).  
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
OC Mammalia; Eutheria; Rodentia; Hystricognathi; Caviidae; Cavia.  
OX NCBI\_TaxID=10141;  
RN [1]  
RP SEQUENCE FROM N.A., AND ALTERNATIVE SPLICING.  
RC TISSUE=Brain, and Liver;  
RX MEDLINE=97236426; PubMed=9116031;  
RA Beck M., Mueller D., Bigl V.;  
RT "Amyloid precursor protein in Guinea pigs - complete cDNA sequence and  
RT alternative splicing.";  
RL Biochim. Biophys. Acta 1351:17-21(1997).  
RN [2]  
RP INTERACTION OF BETA-APP40 WITH APOE.  
RX MEDLINE=98007700; PubMed=9349544;  
RA Martel C.L., Mackic J.B., Matsubara E., Governale S., Miguel C.,  
RA Miao W., McComb J.G., Frangione B., Ghiso J., Zlokovic B.V.;  
RT "Isoform-specific effects of apolipoproteins E2, E3, and E4 on  
RT cerebral capillary sequestration and blood-brain barrier transport of  
RT circulating Alzheimer's amyloid beta.";  
RL J. Neurochem. 69:1995-2004(1997).  
RN [3]  
RP PROCESSING.  
RX MEDLINE=20084499; PubMed=10619481;  
RA Beck M., Brueckner M.K., Holzer M., Kaap S., Pannicke T., Arendt T.,  
RA Bigl V.;  
RT "Guinea-pig primary cell cultures provide a model to study expression  
RT and amyloidogenic processing of endogenous amyloid precursor  
RT protein.";  
RL Neuroscience 95:243-254(2000).  
RN [4]  
RP GAMMA-SECRETASE PROCESSING.  
RX MEDLINE=20576391; PubMed=11035007;  
RA Pinnix I., Musunuru U., Tun H., Sridharan A., Golde T., Eckman C.,  
RA Ziani-Cherif C., Onstead L., Sambamurti K.;  
RT "A novel gamma -secretase assay based on detection of the putative  
RT C-terminal fragment-gamma of amyloid beta protein precursor.";  
RL J. Biol. Chem. 276:481-487(2001).  
CC -!- FUNCTION: Functions as a cell surface receptor and performs  
CC physiological functions on the surface of neurons relevant to  
CC neurite growth, neuronal adhesion and axonogenesis. Involved in  
CC cell mobility and transcription regulation through protein-protein  
CC interactions (By similarity). Can promote transcription activation  
CC through binding to APBB1/Tip60 and inhibit Notch signaling through  
CC interaction with Numb (By similarity). Couples to apoptosis-  
CC inducing pathways such as those mediated by G(O) and JIP (By  
CC similarity). Inhibits G(O) alpha ATPase activity (By similarity).  
CC Acts as a kinesin I membrane receptor, mediating the axonal  
CC transport of beta-secretase and presenilin 1 (By similarity). May  
CC be involved in copper homeostasis/oxidative stress through copper  
CC ion reduction (By similarity). In vitro, copper-metallated APP  
CC induces neuronal death directly or is potentiated through Cu(II)-  
CC mediated low-density lipoprotein oxidation (By similarity). Can

CC regulate neurite outgrowth through binding to components of the  
 CC extracellular matrix such as heparin and collagen I and IV (By  
 CC similarity). The splice isoforms that contain the BPTI domain  
 CC possess protease inhibitor activity (By similarity).  
 CC -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators  
 CC with metal-reducing activity. Bind transient metals such as  
 CC copper, zinc and iron. Beta-amyloid peptides bind to lipoproteins  
 CC and apolipoproteins E and J in the CSF and to HDL particles in  
 CC plasma, inhibiting metal-catalyzed oxidation of lipoproteins.  
 CC -!- FUNCTION: Appicans elicit adhesion of neural cells to the  
 CC extracellular matrix and may regulate neurite outgrowth in the  
 CC brain (By similarity).  
 CC -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved  
 CC peptides, including C31, are potent enhancers of neuronal  
 CC apoptosis (By similarity).  
 CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several  
 CC cytoplasmic proteins, including APBB family members, the APBA  
 CC family, MAPK8IP1, SHC1 and Numb and Dab1 (By similarity). Also  
 CC interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2  
 CC (via its TPR domains), APPBP2 (via BaSS) and DDB1 (By similarity).  
 CC Associates with microtubules in the presence of ATP and in a  
 CC kinesin-dependent manner (By similarity). Soluble Abeta40 binds  
 CC all three isoforms of APOE, in vitro and in vivo. When lipidated,  
 CC ApoE3 appears to be the preferred amyloid binding isoform, while  
 CC the apoE4 isoform-beta-APP40 complex is capable of being  
 CC transported across the blood-brain barrier.  
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface  
 CC protein that rapidly becomes internalized via clathrin-coated pits  
 CC (By similarity). During maturation, the immature APP (N-  
 CC glycosylated in the endoplasmic reticulum) moves to the Golgi  
 CC complex where complete maturation occurs (O-glycosylated and  
 CC sulfated) (By similarity). After alpha-secretase cleavage, soluble  
 CC APP is released into the extracellular space and the C-terminal is  
 CC internalized to endosomes and lysosomes (By similarity). Some APP  
 CC accumulates in secretory transport vesicles leaving the late Golgi  
 CC compartment and returns to the cell surface (By similarity). APP  
 CC sorts to the basolateral surface in epithelial cells (By  
 CC similatity).  
 CC -!- ALTERNATIVE PRODUCTS:  
 CC Event=Alternative splicing; Named isoforms=2;  
 CC Comment=Additional isoforms, missing exons 7,8 and 15, seem to  
 CC exist. The L-isoforms, missing exon 15, are referred to as  
 CC appicans;  
 CC Name=APP770;  
 CC IsoId=Q60495-1; Sequence=Displayed;  
 CC Name=APP695;  
 CC IsoId=Q60495-2; Sequence=VSP\_007221, VSP\_007222;  
 CC -!- TISSUE SPECIFICITY: Isoform APP695 is the major isoform found in  
 CC brain. The longer isoforms containing the BPTI domain are  
 CC predominantly expressed in peripheral organs such as muscle and  
 CC liver.  
 CC -!- INDUCTION: Increased levels during neuronal differentiation.  
 CC -!- DOMAIN: The basolateral sorting signal (BaSS) is required for  
 CC sorting of membrane proteins to the basolateral surface of  
 CC epithelial cells.  
 CC -!- DOMAIN: The NPXY sequence motif found in many tyrosine-  
 CC phosphorylated proteins is required for the specific binding of

CC the PID domain. However additional amino acids either N- or C-  
 CC terminal to the NPXY motif are often required for complete  
 CC interaction. The PID domain-containing proteins which bind APP  
 CC require the YENPTY motif for full interaction. These interactions  
 CC are independent of phosphorylation on the terminal tyrosine  
 CC residue (By similarity). The NPXY site is also involved in  
 CC clathrin-mediated endocytosis.

CC -!- PTM: Proteolytically processed under normal cellular conditions.  
 CC Cleavage by alpha-secretase or alternatively by beta-secretase  
 CC leads to generation and extracellular release of soluble APP  
 CC peptides, S-APP-alpha and S-APP-beta, respectively, and the  
 CC retention of corresponding membrane-anchored C-terminal fragments,  
 CC CTF-alpha and CTF-beta. Subsequent processing of CTF-alpha by  
 CC gamma-secretase yields P3 peptides. This is the major secretory  
 CC pathway and is nonamyloidogenic. Alternatively,  
 CC presenilin/nicastrin-mediated gamma-secretase processing of CTF-  
 CC beta releases the amyloid beta proteins, amyloid-beta 40 (Abeta40)  
 CC and amyloid-beta 42 (Abeta42), major components of amyloid  
 CC plaques, and the corresponding cytotoxic C-terminal fragments  
 CC (CTFs).

CC -!- PTM: Proteolytically cleaved by caspase-3 during neuronal  
 CC apoptosis (By similarity).

CC -!- PTM: N- and O-glycosylated. O-linkage of chondroitin sulfate to  
 CC the L-APP isoforms produces the APP proteoglycan core proteins,  
 CC the appicans (By similarity).

CC -!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and  
 CC serine residues is neuron-specific (By similarity).  
 CC Phosphorylation can affect APP processing, neuronal  
 CC differentiation and interaction with other proteins.

CC -!- PTM: Extracellular binding and reduction of copper, results in a  
 CC corresponding oxidation of Cys-144 and Cys-158, and the formation  
 CC of a disulfide bond (By similarity).

CC -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and  
 CC zinc, can induce histidine-bridging between beta-amyloid molecules  
 CC resulting in beta-amyloid-metal aggregates.

CC -!- SIMILARITY: Belongs to the APP family.

CC -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.

CC -----  
 CC This SWISS-PROT entry is copyright. It is produced through a collaboration  
 CC between the Swiss Institute of Bioinformatics and the EMBL outstation -  
 CC the European Bioinformatics Institute. There are no restrictions on its  
 CC use by non-profit institutions as long as its content is in no way  
 CC modified and this statement is not removed. Usage by and for commercial  
 CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>  
 CC or send an email to [license@isb-sib.ch](mailto:license@isb-sib.ch)).  
 CC -----

DR EMBL; X97631; CAA66230.1; -.  
 DR EMBL; X99198; CAA67589.1; -.  
 DR HSSP; P05067; 1BA4.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR002223; Kunitz\_BPTI.  
 DR Pfam; PF00014; Kunitz\_BPTI; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR PRINTS; PR00759; BASICPTASE.  
 DR ProDom; PD000222; Kunitz\_BPTI; 1.  
 DR SMART; SM00006; A4\_EXTRA; 1.

DR SMART; SM00131; KU; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 DR PROSITE; PS00280; BPTI\_KUNITZ\_1; 1.  
 DR PROSITE; PS50279; BPTI\_KUNITZ\_2; 1.  
 KW Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;  
 KW Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;  
 KW Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;  
 KW Proteoglycan; Alternative splicing; Amyloid.

FT	SIGNAL	1	17	BY SIMILARITY.
FT	CHAIN	18	770	AMYLOID BETA A4 PROTEIN.
FT	CHAIN	18	687	SOLUBLE APP-ALPHA (BY SIMILARITY).
FT	CHAIN	18	671	SOLUBLE APP-BETA (BY SIMILARITY).
FT	CHAIN	672	770	CTF-ALPHA (BY SIMILARITY).
FT	CHAIN	672	713	BETA-AMYLOID PROTEIN 42 (BY SIMILARITY).
FT	CHAIN	672	711	BETA-AMYLOID PROTEIN 40 (BY SIMILARITY).
FT	CHAIN	688	770	CTF-BETA (BY SIMILARITY).
FT	CHAIN	688	713	P3(42) (BY SIMILARITY).
FT	CHAIN	688	711	P3(40) (BY SIMILARITY).
FT	CHAIN	712	770	GAMMA-CTF(59) (BY SIMILARITY).
FT	CHAIN	714	770	GAMMA-CTF(57) (BY SIMILARITY).

Query Match 96.5%; Score 3522.5; DB 1; Length 770;  
 Best Local Similarity 88.2%; Pred. No. 2.1e-165;  
 Matches 679; Conservative 7; Mismatches 9; Indels 75; Gaps 1;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRILNMHMNVQNGKWDSDPSGTK	60
		:       :	
Db	1	MLPSLALLLLTTWTARALEVPTDGNAGLLAEPQIAMFCGKLNHMHMNVQNGKWEVDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVPIPYRCLVG	120
		:	
Db	61	TCIGSKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRSRKQCKTHPHFVPIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
		:                     :	
Db	181	GVEFVCCPLAEESDNIDSADAEEDDSDVWWGGADTDYADGSEDKVVEVAEEEEVADVVEE	240
Qy	241	EADDDDEDEDGDEVEEEAEEPVEEATERTTSIATTTTTTTESVEEVVR-----	288
		:	
Db	241	EADDDDEDVEDGDEVEEEAEEPVEEATEKTTTSIATTTTTTTESVEEVVREVCSEQAETGPC	300
Qy	289	-----	288
Db	301	RSMISRWFYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMVCGSVMSQNLLKTSGEVPSQG	360
Qy	289	---VPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQA	345
		:	
Db	361	PVKLPPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQA	420
Qy	346	KNLPKADKKAVIQHFQEKVESLEQEAAANERQQVLVETHMARVEAMLNDRRRRLALENYITAL	405
Db	421	KNLPKADKKAVIQHFQEKVESLEQEAAANERQQVLVETHMARVEAMLNDRRRRLALENYITAL	480

Qy 406 QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER 465  
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||  
 Db 481 QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER 540  
 Qy 466 MNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTET 525  
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||  
 Db 541 MNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTET 600  
 Qy 526 KTTVELLPVNGEFSLDDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTN 585  
 |||||||||||||||| || ||||||||||||||||||||||||||||||||  
 Db 601 KTTVELLPVNGEFSLDDLQPWHPFGVDSVPANTENEVEPVDARPAADRGLTTRPGSGLTN 660  
 Qy 586 IKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITL 645  
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||  
 Db 661 IKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITL 720  
 Qy 646 VMLKKKQYTSIHGVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695  
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||  
 Db 721 VMLKKKQYTSIHGVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 770

RESULT 6

A4\_MOUSE

ID A4\_MOUSE STANDARD; PRT; 770 AA.  
 AC P12023; P97487; P97942; Q99K32;  
 DT 01-OCT-1989 (Rel. 12, Created)  
 DT 10-OCT-2003 (Rel. 42, Last sequence update)  
 DT 10-OCT-2003 (Rel. 42, Last annotation update)  
 DE Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease  
 DE amyloid protein homolog) (Amyloidogenic glycoprotein) (AG) [Contains:  
 DE Soluble APP-alpha (S-APP-alpha); Soluble APP-beta (S-APP-beta); C99  
 DE (APP-C99); Beta-amyloid protein 42 (Beta-APP42); Beta-amyloid protein  
 DE 40 (Beta-APP40); C83; P3(42); P3(40); Gamma-CTF(59) (Gamma-secretase  
 DE C-terminal fragment 59) (Amyloid intracellular domain 59) (AID(59))  
 DE (APP-C59); Gamma-CTF(57) (Gamma-secretase C-terminal fragment 57)  
 DE (Amyloid intracellular domain 57) (AID(57)) (APP-C57); Gamma-CTF(50)  
 DE (Gamma-secretase C-terminal fragment 50) (Amyloid intracellular domain  
 DE 50) (AID(50)); C31].  
 GN APP.  
 OS Mus musculus (Mouse).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.  
 OX NCBI\_TaxID=10090;  
 RN [1]  
 RP SEQUENCE FROM N.A. (ISOFORM APP695).  
 RC TISSUE=Brain;  
 RX MEDLINE=88106489; PubMed=3322280;  
 RA Yamada T., Sasaki H., Furuya H., Miyata T., Goto I., Sakaki Y.;  
 RT "Complementary DNA for the mouse homolog of the human amyloid beta  
 RT protein precursor."  
 RL Biochem. Biophys. Res. Commun. 149:665-671(1987).  
 RN [2]  
 RP REVISIONS.  
 RA Yamada T.;  
 RL Submitted (MAR-1988) to the EMBL/GenBank/DDBJ databases.  
 RN [3]

RP SEQUENCE FROM N.A. (ISOFORM APP695).  
 RC STRAIN=BALB/c; TISSUE=Brain;  
 RX MEDLINE=92096458; PubMed=1756177;  
 RA de Strooper B., van Leuven F., van den Berghe H.;  
 RT "The amyloid beta protein precursor or proteinase nexin II from mouse  
 RT is closer related to its human homolog than previously reported.";  
 RL Biochim. Biophys. Acta 1129:141-143(1991).  
 RN [4]  
 RP SEQUENCE FROM N.A. (ISOFORM APP695).  
 RC STRAIN=SAMP8; TISSUE=Hippocampus;  
 RX MEDLINE=21130647; PubMed=11235921;  
 RA Kumar V.B., Vyas K., Franko M., Choudhary V., Buddhiraju C.,  
 RA Alvarez J., Morley J.E.;  
 RT "Molecular cloning, expression, and regulation of hippocampal amyloid  
 RT precursor protein of senescence accelerated mouse (SAMP8).";  
 RL Biochem. Cell Biol. 79:57-67(2001).  
 RN [5]  
 RP SEQUENCE OF 1-19 FROM N.A.  
 RX MEDLINE=92209998; PubMed=1555768;  
 RA Izumi R., Yamada T., Yoshikai S.I., Sasaki H., Hattori M.,  
 RA Sakai Y.;  
 RT "Positive and negative regulatory elements for the expression of the  
 RT Alzheimer's disease amyloid precursor-encoding gene in mouse.";  
 RL Gene 112:189-195(1992).  
 RN [6]  
 RP PARTIAL SEQUENCE FROM N.A. (ISOFORM APP770).  
 RC TISSUE=Breast tumor;  
 RX MEDLINE=22388257; PubMed=12477932;  
 RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,  
 RA Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,  
 RA Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,  
 RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,  
 RA Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,  
 RA Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,  
 RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,  
 RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,  
 RA Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,  
 RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,  
 RA Villalón D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,  
 RA Fahey J., Helton E., Kettelman M., Madan A., Rodrigues S., Sanchez A.,  
 RA Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,  
 RA Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,  
 RA Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,  
 RA Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,  
 RA Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;  
 RT "Generation and initial analysis of more than 15,000 full-length human  
 RT and mouse cDNA sequences.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).  
 RN [7]  
 RP SEQUENCE OF 281-380 FROM N.A., AND ALTERNATIVE SPLICING.  
 RC TISSUE=Brain, and Kidney;  
 RX MEDLINE=89149813; PubMed=2493250;  
 RA Yamada T., Sasaki H., Dohura K., Goto I., Sakaki Y.;  
 RT "Structure and expression of the alternatively-spliced forms of mRNA  
 RT for the mouse homolog of Alzheimer's disease amyloid beta protein  
 RT precursor.";  
 RL Biochem. Biophys. Res. Commun. 158:906-912(1989).

RN [8]  
 RP SEQUENCE OF 289-364 FROM N.A.  
 RC STRAIN=CD-1; TISSUE=Placenta;  
 RX MEDLINE=89345111; PubMed=2569710;  
 RA Fukuchi K., Martin G.M., Deeb S.S.;  
 RT "Sequence of the protease inhibitor domain of the A4 amyloid protein  
 RT precursor of *Mus domesticus*.";  
 RL Nucleic Acids Res. 17:5396-5396(1989).  
 RN [9]  
 RP SEQUENCE OF 656-737 FROM N.A.  
 RC STRAIN=129/Sv;  
 RA Wragg M.A., Busfield F., Duff K., Korenblat K., Capecchi M.,  
 RA Loring J.F., Goate A.M.;  
 RT "Introduction of six mutations into the mouse genome using 'Hit and  
 RT Run' gene-targeting: introduction of familial Alzheimer's disease  
 RT mutations into the mouse amyloid precursor protein gene and  
 RT humanization of the A-beta fragment.";  
 RL Submitted (DEC-1996) to the EMBL/GenBank/DDBJ databases.  
 RN [10]  
 RP TISSUE SPECIFICITY OF ALTERNATIVE SPLICED FORMS.  
 RX MEDLINE=93287808; PubMed=8510506;  
 RA Sola C., Mengod G., Ghetti B., Palacios J.M., Triarhou L.C.;  
 RT "Regional distribution of the alternatively spliced isoforms of beta  
 RT APP RNA transcript in the brain of normal, heterozygous and  
 RT homozygous weaver mutant mice as revealed by in situ hybridization  
 RT histochemistry.";  
 RL Brain Res. Mol. Brain Res. 17:340-346(1993).  
 RN [11]  
 RP INTERACTION WITH KNS2.  
 RX MEDLINE=21010507; PubMed=11144355;  
 RA Kamal A., Stokin G.B., Yang Z., Xia C.-H., Goldstein L.S.;  
 RT "Axonal transport of amyloid precursor protein is mediated by direct  
 RT binding to the kinesin light chain subunit of kinesin-I.";  
 RL Neuron 28:449-459(2000).  
 RN [12]  
 RP C-TERMINAL PROTEIN-PROTEIN INTERACTIONS, AND MUTAGENESIS OF TYR-728;  
 RP THR-743; TYR-757; ASN-759 AND TYR-762.  
 RX MEDLINE=21408156; PubMed=11517249;  
 RA Matsuda S., Yasukawa T., Homma Y., Ito Y., Niikura T., Hiraki T.,  
 RA Hirai S., Ohno S., Kita Y., Kawasumi M., Kouyama K., Yamamoto T.,  
 RA Kyriakis J.M., Nishimoto I.;  
 RT "C-jun N-terminal kinase (JNK)-interacting protein-1b/islet-brain-1  
 RT scaffolds Alzheimer's amyloid precursor protein with JNK.";  
 RL J. Neurosci. 21:6597-6607(2001).  
 RN [13]  
 RP INTERACTION WITH MAPK8IP1, AND PHOSPHORYLATION.  
 RX MEDLINE=22028091; PubMed=11912189;  
 RA Taru H., Iijima K.-I., Hase M., Kirino Y., Yagi Y., Suzuki T.;  
 RT "Interaction of Alzheimer's beta-amyloid precursor family proteins  
 RT with scaffold proteins of the JNK signaling cascade.";  
 RL J. Biol. Chem. 277:20070-20078(2002).  
 RN [14]  
 RP INTERACTION OF CTF PEPTIDES WITH NUMB.  
 RX MEDLINE=22008109; PubMed=12011466;  
 RA Roncarati R., Sestan N., Scheinfeld M.H., Berechid B.E., Lopez P.A.,  
 RA Meucci O., McGlade J.C., Rakic P., D'Adamio L.;  
 RT "The gamma-secretase-generated intracellular domain of beta-amyloid

RT precursor protein binds Numb and inhibits Notch signaling.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 99:7102-7107(2002).  
 RN [15]  
 RP GAMMA-SECRETASE PROCESSING, AND INTERACTION WITH APBB1.  
 RX MEDLINE=21437805; PubMed=11553691;  
 RA Cupers P., Orlans I., Craessaerts K., Annaert W., De Strooper B.;  
 RT "The amyloid precursor protein (APP)-cytoplasmic fragment generated by  
 RT gamma-secretase is rapidly degraded but distributes partially in a  
 RT nuclear fraction of neurones in culture.";  
 RL J. Neurochem. 78:1168-1178(2001).  
 CC -!- FUNCTION: Functions as a cell surface receptor and performs  
 CC physiological functions on the surface of neurons relevant to  
 CC neurite growth, neuronal adhesion and axonogenesis. Involved in  
 CC cell mobility and transcription regulation through protein-protein  
 CC interactions. Can promote transcription activation through binding  
 CC to APBB1/Tip60 and inhibit Notch signaling through interaction  
 CC with Numb. Couples to apoptosis-inducing pathways such as those  
 CC mediated by G(0) and JIP. Inhibits G(0) alpha ATPase activity (By  
 CC similarity). Acts as a kinesin I membrane receptor, mediating the  
 CC axonal transport of beta-secretase and presenilin 1. May be  
 CC involved in copper homeostasis/oxidative stress through copper ion  
 CC reduction. Can regulate neurite outgrowth through binding to  
 CC components of the extracellular matrix such as heparin and  
 CC collagen I and IV (By similarity). The splice isoforms that  
 CC contain the BPTI domain possess protease inhibitor activity (By  
 CC similarity).  
 CC -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators  
 CC with metal-reducing activity. Bind transient metals such as  
 CC copper, zinc and iron. Rat and mouse beta-amyloid peptides bind  
 CC only weakly transient metals and have little reducing activity due  
 CC to substitutions of transient metal chelating residues. Beta-APP42  
 CC may activate mononuclear phagocytes in the brain and elicit  
 CC inflammatory responses. Promotes both tau aggregation and TPK II-  
 CC mediated phosphorylation (By similarity).  
 CC -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved  
 CC peptides, including C31, are potent enhancers of neuronal  
 CC apoptosis.  
 CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several  
 CC cytoplasmic proteins, including APBB family members, the APBA  
 CC family, MAPK8IP1, SHC1, Numb and Dab1. Binding to Dab1 inhibits  
 CC its serine phosphorylation. Also interacts with GPCR-like protein  
 CC BPP, FPRL1, APPBP1, IB1, KNS2 (via its TPR domains), APPBP2 (via  
 CC BaSS) and DDB1 (By similarity). In vitro, it binds MAPT via the  
 CC MT-binding domains (By similarity). Associates with microtubules  
 CC in the presence of ATP and in a kinesin-dependent manner (By  
 CC similarity). Interacts, through a C-terminal domain, with GNAO1  
 CC (By similarity). Amyloid beta-42 binds CHRNA7 in hippocampal  
 CC neurons (By similarity). Beta-amyloid associates with HADH2 (By  
 CC similarity).  
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface  
 CC protein that rapidly becomes internalized via clathrin-coated  
 CC pits. During maturation, the immature APP (N-glycosylated in the  
 CC endoplasmic reticulum) moves to the Golgi complex where complete

Query Match 95.7%; Score 3493.5; DB 1; Length 770;  
 Best Local Similarity 87.8%; Pred. No. 5.5e-164;  
 Matches 676; Conservative 6; Mismatches 13; Indels 75; Gaps 1;





AC P08592;  
 DT 01-AUG-1988 (Rel. 08, Created)  
 DT 01-DEC-1992 (Rel. 24, Last sequence update)  
 DT 10-OCT-2003 (Rel. 42, Last annotation update)  
 DE Amyloid beta A4 protein precursor (APP) (Alzheimer's disease amyloid  
 DE protein homolog) (Amyloidogenic glycoprotein) (AG) [Contains: Soluble  
 DE APP-alpha (S-APP-alpha); Soluble APP-beta (S-APP-beta); C99; Beta-  
 DE amyloid protein 42 (Beta-APP42); Beta-amyloid protein 40 (Beta-APP40);  
 DE C83; P3(42); P3(40); Gamma-CTF(59) (Gamma-secretase C-terminal  
 DE fragment 59); Gamma-CTF(57) (Gamma-secretase C-terminal fragment 57);  
 DE Gamma-CTF(50) (Gamma-secretase C-terminal fragment 50); C31].  
 GN APP.  
 OS Rattus norvegicus (Rat).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.  
 OX NCBI\_TaxID=10116;  
 RN [1]  
 RP SEQUENCE FROM N.A. (ISOFORM APP695).  
 RC TISSUE=Brain;  
 RX MEDLINE=88312583; PubMed=2900758;  
 RA Shivers B.D., Hilbich C., Multhaup G., Salbaum J.M., Beyreuther K.,  
 RA Seeburg P.H.;  
 RT "Alzheimer's disease amyloidogenic glycoprotein: expression pattern  
 RT in rat brain suggests a role in cell contact.";  
 RL EMBO J. 7:1365-1370(1988).  
 RN [2]  
 RP SEQUENCE OF 289-364 FROM N.A.  
 RC TISSUE=Liver;  
 RX MEDLINE=89183625; PubMed=2648331;  
 RA Kang J., Mueller-Hill B.;  
 RT "The sequence of the two extra exons in rat preA4.";  
 RL Nucleic Acids Res. 17:2130-2130(1989).  
 RN [3]  
 RP SEQUENCE OF 720-730, AND MASS SPECTROMETRY.  
 RX MEDLINE=21443797; PubMed=11483588;  
 RA Gu Y., Misonou H., Sato T., Dohmae N., Takio K., Ihara Y.;  
 RT "Distinct intramembrane cleavage of the beta-amyloid precursor protein  
 RT family resembling gamma-secretase-like cleavage of Notch.";  
 RL J. Biol. Chem. 276:35235-35238(2001).  
 RN [4]  
 RP ALTERNATIVE SPLICING.  
 RX MEDLINE=96187032; PubMed=8624099;  
 RA Sandbrink R., Masters C.L., Beyreuther K.;  
 RT "APP gene family. Alternative splicing generates functionally related  
 RT isoforms.";  
 RL Ann. N.Y. Acad. Sci. 777:281-287(1996).  
 RN [5]  
 RP TISSUE SPECIFICITY OF APPICAN.  
 RX MEDLINE=95263526; PubMed=7744833;  
 RA Shioi J., Pangalos M.N., Ripellino J.A., Vassilacopoulou D.,  
 RA Mytilineou C., Margolis R.U., Robakis N.K.;  
 RT "The Alzheimer amyloid precursor proteoglycan (appican) is present in  
 RT brain and is produced by astrocytes but not by neurons in primary  
 RT neural cultures.";  
 RL J. Biol. Chem. 270:11839-11844(1995).  
 RN [6]  
 RP TISSUE SPECIFICITY OF ISOFORMS.

RX MEDLINE=97150061; PubMed=8996834;  
 RA Sandbrink R., Monning U., Masters C.L., Beyreuther K.;  
 RT "Expression of the APP gene family in brain cells, brain development  
 RT and aging.";  
 RL Gerontology 43:119-131(1997).  
 RN [7]  
 RP INTERACTION WITH DDB1, AND MUTAGENESIS OF TYR-757; ASN-759 AND  
 RP TYR-762.  
 RX MEDLINE=99127916; PubMed=9930726;  
 RA Watanabe T., Sukegawa J., Tomita S., Iijima K.-I., Oguchi S.,  
 RA Suzuki T., Nairn A.C., Greengard P.;  
 RT "A 127-kDa protein (UV-DDB) binds to the cytoplasmic domain of the  
 RT Alzheimer's amyloid precursor protein.";  
 RL J. Neurochem. 72:549-556(1999).  
 RN [8]  
 RP INTERACTION WITH GNAO1, AND MUTAGENESIS OF 732-HIS-HIS-733.  
 RX MEDLINE=99162676; PubMed=10024358;  
 RA Brouillet E., Trembleau A., Galanaud D., Volovitch M., Bouillot C.,  
 RA Valenza C., Prochiantz A., Allinquant B.;  
 RT "The amyloid precursor protein interacts with Go heterotrimeric  
 RT protein within a cell compartment specialized in signal  
 RT transduction.";  
 RL J. Neurosci. 19:1717-1727(1999).  
 RN [9]  
 RP CHARACTERISTICS OF APPICAN, AND MUTAGENESIS OF SER-656.  
 RX MEDLINE=95256193; PubMed=7737970;  
 RA Pangalos M.N., Efthimiopoulos S., Shioi J., Robakis N.K.;  
 RT "The chondroitin sulfate attachment site of appican is formed by  
 RT splicing out exon 15 of the amyloid precursor gene.";  
 RL J. Biol. Chem. 270:10388-10391(1995).  
 RN [10]  
 RP BETA-AMYLOID METAL-BINDING.  
 RX MEDLINE=99316162; PubMed=10386999;  
 RA Huang X., Atwood C.S., Hartshorn M.A., Multhaup G., Goldstein L.E.,  
 RA Scarpa R.C., Cuajungco M.P., Gray D.N., Lim J., Moir R.D., Tanzi R.E.,  
 RA Bush A.I.;  
 RT "The A beta peptide of Alzheimer's disease directly produces hydrogen  
 RT peroxide through metal ion reduction.";  
 RL Biochemistry 38:7609-7616(1999).  
 RN [11]  
 RP BETA-AMYLOID ZINC BINDING.  
 RX MEDLINE=99343552; PubMed=10413512;  
 RA Liu S.T., Howlett G., Barrow C.J.;  
 RT "Histidine-13 is a crucial residue in the zinc ion-induced aggregation  
 RT of the A beta peptide of Alzheimer's disease.";  
 RL Biochemistry 38:9373-9378(1999).  
 RN [12]  
 RP IMPORTANCE OF GLY-704 IN FREE RADICAL PROPAGATION, AND MUTAGENESIS OF  
 RP GLY-704.  
 RX MEDLINE=21956095; PubMed=11959460;  
 RA Kanski J., Varadarajan S., Aksenova M., Butterfield D.A.;  
 RT "Role of glycine-33 and methionine-35 in Alzheimer's amyloid beta-  
 RT peptide 1-42-associated oxidative stress and neurotoxicity.";  
 RL Biochim. Biophys. Acta 1586:190-198(2001).  
 RN [13]  
 RP PHOSPHORYLATION.  
 RX MEDLINE=97239592; PubMed=9085254;

RA Oishi M., Nairn A.C., Czernik A.J., Lim G.S., Isohara T., Gandy S.E.,  
 RA Greengard P., Suzuki T.;  
 RT "The cytoplasmic domain of Alzheimer's amyloid precursor protein is  
 RT phosphorylated at Thr654, Ser655, and Thr668 in adult rat brain and  
 RT cultured cells.";  
 RL Mol. Med. 3:111-123(1997).  
 RN [14]  
 RP PHOSPHORYLATION ON SER-730.  
 RX MEDLINE=99262094; PubMed=10329382;  
 RA Isohara T., Horiuchi A., Watanabe T., Ando K., Czernik A.J., Uno I.,  
 RA Greengard P., Nairn A.C., Suzuki T.;  
 RT "Phosphorylation of the cytoplasmic domain of Alzheimer's beta-amyloid  
 RT precursor protein at Ser655 by a novel protein kinase.";  
 RL Biochem. Biophys. Res. Commun. 258:300-305(1999).  
 RN [15]  
 RP PHOSPHORYLATION, INDUCTION, SUBCELLULAR LOCATION, AND MUTAGENESIS OF  
 RP THR-743.  
 RX MEDLINE=99274744; PubMed=10341243;  
 RA Ando K., Oishi M., Takeda S., Iijima K.-I., Isohara T., Nairn A.C.,  
 RA Kirino Y., Greengard P., Suzuki T.;  
 RT "Role of phosphorylation of Alzheimer's amyloid precursor protein  
 RT during neuronal differentiation.";  
 RL J. Neurosci. 19:4421-4427(1999).  
 RN [16]  
 RP PHOSPHORYLATION ON THR-743.  
 RX MEDLINE=20396183; PubMed=10936190;  
 RA Iijima K.-I., Ando K., Takeda S., Satoh Y., Seki T., Itohara S.,  
 RA Greengard P., Kirino Y., Nairn A.C., Suzuki T.;  
 RT "Neuron-specific phosphorylation of Alzheimer's beta-amyloid precursor  
 RT protein by cyclin-dependent kinase 5.";  
 RL J. Neurochem. 75:1085-1091(2000).  
 RN [17]  
 RP CARBOHYDRATE STRUCTURE OF APPICAN.  
 RX MEDLINE=21463085; PubMed=11479316;  
 RA Tsuchida K., Shioi J., Yamada S., Boghosian G., Wu A., Cai H.,  
 RA Sugahara K., Robakis N.K.;  
 RT "Appican, the proteoglycan form of the amyloid precursor protein,  
 RT contains chondroitin sulfate E in the repeating disaccharide region  
 RT and 4-O-sulfated galactose in the linkage region.";  
 RL J. Biol. Chem. 276:37155-37160(2001).  
 CC -!- FUNCTION: Functions as a cell surface receptor and performs  
 CC physiological functions on the surface of neurons relevant to  
 CC neurite growth, neuronal adhesion and axonogenesis. Involved in  
 CC cell mobility and transcription regulation through protein-protein  
 CC interactions (By similarity). Can promote transcription activation  
 CC through binding to APBB1/Tip60 and inhibit Notch signaling through  
 CC interaction with Numb (By similarity). Couples to apoptosis-  
 CC inducing pathways such as those mediated by G(0) and JIP. Inhibits  
 CC G(0) alpha ATPase activity. Acts as a kinesin I membrane receptor,  
 CC mediating the axonal transport of beta-secretase and presenilin 1  
 CC (By similarity). May be involved in copper homeostasis/oxidative  
 CC stress through copper ion reduction. Can regulate neurite  
 CC outgrowth through binding to components of the extracellular  
 CC matrix such as heparin and collagen I and IV (By similarity). The  
 CC splice isoforms that contain the BPTI domain possess protease  
 CC inhibitor activity (By similarity).  
 CC -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators

CC with metal-reducing activity. Bind transient metals such as  
 CC copper, zinc and iron. Rat and mouse beta-amyloid peptides bind  
 CC only weakly transient metals and have little reducing activity due  
 CC to substitutions of transient metal chelating residues. Beta-APP42  
 CC may activate mononuclear phagocytes in the brain and elicit  
 CC inflammatory responses. Promotes both tau aggregation and TPK II-  
 CC mediated phosphorylation (By similarity).  
 CC -!- FUNCTION: Appicans elicit adhesion of neural cells to the  
 CC extracellular matrix and may regulate neurite outgrowth in the  
 CC brain.  
 CC -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved  
 CC peptides, including C31, are potent enhancers of neuronal  
 CC apoptosis (By similarity).  
 CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several  
 CC cytoplasmic proteins, including APBB family members, the APBA  
 CC family, MAPK8IP1, SHC1 and Numb and Dab1 (By similarity). Binding  
 CC to Dab1 inhibits its serine phosphorylation (By similarity). Also  
 CC interacts with GPCR-like protein BPP, FPR1, APPBP1, IB1, KNS2  
 CC (via its TPR domains), APPBP2 (via BaSS) (By similarity) and DDB1.  
 CC In vitro, it binds MAPT via the MT-binding domains (By  
 CC similarity). Associates with microtubules in the presence of ATP  
 CC and in a kinesin-dependent manner (By similarity). Interacts,  
 CC through a C-terminal domain, with GNAO1. Amyloid beta-42 binds  
 CC CHRNA7 in hippocampal neurons (By similarity). Beta-amyloid  
 CC associates with HADH2 (By similarity).  
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface  
 CC protein that rapidly becomes internalized via clathrin-coated  
 CC pits. During maturation, the immature APP (N-glycosylated in the

Query Match 95.7%; Score 3493.5; DB 1; Length 770;  
 Best Local Similarity 87.7%; Pred. No. 5.5e-164;  
 Matches 675; Conservative 8; Mismatches 12; Indels 75; Gaps 1;

```

Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
      ||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      1 MLPSLALLLLAAWTVRALEVPTDGNAGLLAEPQIAMFCGKLNMHMNVQNGKWESDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
      ||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db     61 TCIGTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHTHVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
      ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
      ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    181 GVEFVCCPLAEESDSIDSADAEEEDSDVWVGADTDYADGGEDKVVEVAEEEEVADVEEEE 240

Qy    241 EADDDDEDDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVR----- 288
      ||: |||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    241 EAEDDEDVEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVREVCSEQAETGPC 300

Qy    289 ----- 288

Db    301 RAMISRWFVDVTEGKCAPFFYGGCGGNRNNFDTEEYCMVCGSVSSQSLIKTTSEPLPQD 360

```

Qy	289	---VPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQA	345
		:	
Db	361	PVKLPPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQA	420
Qy	346	KNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITAL	405
Db	421	KNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITAL	480
Qy	406	QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER	465
Db	481	QAVPPRPHHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER	540
Qy	466	MNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSLTET	525
Db	541	MNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSLTET	600
Qy	526	KTTVELLPVNGEFSLDDLQPPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTN	585
Db	601	KTTVELLPVNGEFSLDDLQPPWHPFGVDSVPANTENEVEPVDARPAADRGLTTRPGSGLTN	660
Qy	586	IKTEEISEVKMDAEFRHDSGYEVHHQKLFFAEDVGSNKGAIIGLMVGGVVIATVIVITL	645
		:	
Db	661	IKTEEISEVKMDAEFGHDSGFVVRHQKLFFAEDVGSNKGAIIGLMVGGVVIATVIVITL	720
Qy	646	VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQQMN	695
Db	721	VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQQMN	770

RESULT 8

A4\_TETFL

ID A4\_TETFL STANDARD; PRT; 780 AA.

AC O73683;

DT 10-OCT-2003 (Rel. 42, Created)

DT 10-OCT-2003 (Rel. 42, Last sequence update)

DT 10-OCT-2003 (Rel. 42, Last annotation update)

DE Alzheimer's disease amyloid A4 protein homolog precursor [Contains:

DE Beta-amyloid protein (Beta-APP) (A-beta)].

GN APP.

OS Tetraodon fluviatilis (Puffer fish).

OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

OC Actinopterygii; Neopterygii; Teleostei; Euteleostei; Neoteleostei;

OC Acanthomorpha; Acanthopterygii; Percomorpha; Tetraodontiformes;

OC Tetradontoidea; Tetraodontidae; Tetraodon.

OX NCBI\_TaxID=47145;

RN [1]

RP SEQUENCE FROM N.A.

RX MEDLINE=98252138; PubMed=9599080;

RA Villard L., Tassone F., Crnogorac-Jurcevic T., Clancy K., Gardiner K.;

RT "Analysis of pufferfish homologues of the AT-rich human APP gene.";

RL Gene 210:17-24(1998).

CC -!- FUNCTION: Functional neuronal receptor which couples to

CC intracellular signaling pathway through the GTP-binding protein

CC G(O) (By similarity).

CC -!- SUBCELLULAR LOCATION: Type I membrane protein.

CC -!- SIMILARITY: Belongs to the APP family.

CC -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.

```

CC -----
CC This SWISS-PROT entry is copyright. It is produced through a collaboration
CC between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC the European Bioinformatics Institute. There are no restrictions on its
CC use by non-profit institutions as long as its content is in no way
CC modified and this statement is not removed. Usage by and for commercial
CC entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC or send an email to license@isb-sib.ch).
CC -----
DR EMBL; AF018165; AAC41275.1; -.
DR HSSP; P05067; 1HZ3.
DR InterPro; IPR008155; A4_APP.
DR InterPro; IPR008154; A4_extra.
DR InterPro; IPR001255; Beta-APP.
DR InterPro; IPR002223; Kunitz_BPTI.
DR Pfam; PF02177; A4_EXTRA; 1.
DR Pfam; PF03494; Beta-APP; 1.
DR Pfam; PF00014; Kunitz_BPTI; 1.
DR PRINTS; PR00203; AMYLOIDA4.
DR PRINTS; PR00759; BASICPTASE.
DR ProDom; PD000222; Kunitz_BPTI; 1.
DR SMART; SM00006; A4_EXTRA; 1.
DR SMART; SM00131; KU; 1.
DR PROSITE; PS00319; A4_EXTRA; 1.
DR PROSITE; PS00320; A4_INTRA; 1.
DR PROSITE; PS00280; BPTI_KUNITZ_1; FALSE_NEG.
DR PROSITE; PS00279; BPTI_KUNITZ_2; 1.
KW Glycoprotein; Amyloid; Neurone; Transmembrane; Signal;
KW Serine protease inhibitor.
FT SIGNAL 1 18 POTENTIAL.
FT CHAIN 19 780 ALZHEIMER'S DISEASE AMYLOID A4 PROTEIN
FT HOMOLOG.
FT CHAIN 682 724 BETA-AMYLOID PROTEIN (POTENTIAL).
FT DOMAIN 19 711 EXTRACELLULAR (POTENTIAL).
FT TRANSMEM 712 732 POTENTIAL.
FT DOMAIN 733 780 CYTOPLASMIC (POTENTIAL).
FT DOMAIN 323 382 BPTI/KUNITZ INHIBITOR.
FT SITE 769 772 CLATHRIN-BINDING (BY SIMILARITY).
FT DISULFID 327 378 BY SIMILARITY.
FT DISULFID 336 361 BY SIMILARITY.
FT CARBOHYD 560 560 N-LINKED (GLCNAC. . .) (POTENTIAL).
SQ SEQUENCE 780 AA; 88238 MW; 60071BE94520191D CRC64;

```

```

Query Match 70.5%; Score 2573; DB 1; Length 780;
Best Local Similarity 65.4%; Pred. No. 6e-119;
Matches 513; Conservative 71; Mismatches 94; Indels 106; Gaps 10;

```

```

Qy 7 LLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGKTCTIDTK 66
   |||:| : | |||| : |||||:||||:|:|:|:|:|:|:|:|:|:|
Db 8 LLLVAAASTLAAEVPTDVSMLLAEPQVAMFCGKINMHINVQSGKWE PDPSGKTCIGTK 67

Qy 67 EGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVGEFVSDA 126
   |||||:|||||:|||||:|||||:|:|:|:|:|:|:|:|:|:|
Db 68 EGILQYCQEVYPELQITNVVEANQPVSIQNWCKKGRKQCRSHMHIVVPYRCLVGEFVSDA 127

Qy 127 LLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEFVC 186
   |||||:|||||:|||||:|:|:|:|:|:|:|:|:|:|

```

Db 128 LLVPDKCKFLHQERMNQCESHLHWHTVAKESCGDRAMNLHDYGMLLPCGIDRFRGVEFVC 187

Qy 187 CPLAEESDNVDSADAEEDDSDVWVGADTDYADGS-----EDKVVEVAEEE 232  
 || || :|| : : ||||| ||:| | ||| ||

Db 188 CP-AEAERDMNSTEKDADDSDVWVGADNDYSNSMVREPEPAEQQEETRPSVVEEEEEEG 246

Qy 233 EVAEEVEEEE-----ADDEDEDGDEVEEEAEPEYEEATERTTSIA 273  
 |||: :|| | ||:|:| | |: | :| | ||:|

Db 247 EVAQEDDEEEVLDTDQDGDGEEDHEAADDEEEEDVDEIDAFGESDDVDADPTTNVA 306

Qy 274 ---TTTTTTTSESVEEVVR----- 288  
 ||||| |||||

Db 307 MTTTTTTTTTSESVEEVVRMFCWAHADTGPCTASMPSWYFDAVDGRTMYELMYGGCGNMN 366

Qy 289 -----VPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQ 333  
 ||| |:|||| | ||| ||||| ||||| ||||| ||||| |||||

Db 367 NFESEYCLSVCSVPTDMPSSPDAVDHYLETPADENEHAHFQKAKESLEAKHRERMSQ 426

Qy 334 VMREWEAAERQAKNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDR 393  
 ||||| |||||:|||| || |||||:|||||:|||||:|||||:|||||

Db 427 VMREWEAAERQAKNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEALLNDR 486

Qy 394 RRLALENYITALQAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRS 453  
 |||||:|||| | |||||:||||| ||||| ||||| ||||| ||||| ||||| |||||

Db 487 RRLALENYITALQDPPRPRHVFSLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRP 546

Qy 454 QVMTHLRVIYERMNQSLSLYNVPAVAEEIQDEVDLLQKEQNYSDVLANMISEPRISY 513  
 |:|||| | |||| | || || |:|:|:| | |||:| | |||: |||: |||: |||:

Db 547 QVLTHLRVIEERMNQSLGLLYKVPGVADDIQDQV-ELLQREQAEMAQQLANLQTDVRVSY 605

Qy 514 GNDALMPSLTETKTTVELLPVNGEFSLDDLQPDWH--SFGADSVANTENEVEPVDARPA 571  
 ||||| :|| | :| : | || | |||:||||:|

Db 606 GNDALMPDQELGDGQADLLP--QEDTLGGVGFVHPESFN----QLNTENQVEPVDSPRPTF 659

Qy 572 DRGLTTRPGSGLTNIKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLM 631  
 :||: ||| :| | : |:|:| | : | ||||| ||||| ||||| ||||| |||||

Db 660 ERGVPTRP---VTGKSMEAVPELMEATEDRQSTYEYVHHQKLVFFAEDVGSNKGAIIGLM 716

Qy 632 VGGVVIATVIVITLVMLKKKQYTSIHGVEVDAAVTPEERHLSKMQQNGYENPTYKFFE 691  
 ||||| |||||:|||||:| ||||| ||||| ||||| ||||| ||||| ||||| |||||

Db 717 VGGVVIATVIVITLVMLRKKQYTSIHGVEVDAAVTPEERHLSKMQQNGYENPTYKFFE 776

Qy 692 QMQN 695  
 ||||

Db 777 QMQN 780

RESULT 9

A4\_FUGRU

ID A4\_FUGRU STANDARD; PRT; 737 AA.

AC 093279;

DT 10-OCT-2003 (Rel. 42, Created)

DT 10-OCT-2003 (Rel. 42, Last sequence update)

DT 10-OCT-2003 (Rel. 42, Last annotation update)

DE Alzheimer's disease amyloid A4 protein homolog precursor [Contains:

DE Beta-amyloid protein (Beta-APP) (A-beta)].

GN APP.



OS Fugu rubripes (Japanese pufferfish) (Takifugu rubripes).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Actinopterygii; Neopterygii; Teleostei; Euteleostei; Neoteleostei;  
 OC Acanthomorpha; Acanthopterygii; Percomorpha; Tetraodontiformes;  
 OC Tetradontoidea; Tetraodontidae; Takifugu.  
 OX NCBI\_TaxID=31033;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RX MEDLINE=98252138; PubMed=9599080;  
 RA Villard L., Tassone F., Crnogorac-Jurcevic T., Clancy K., Gardiner K.;  
 RT "Analysis of pufferfish homologues of the AT-rich human APP gene.";   
 RL Gene 210:17-24(1998).  
 CC -!- FUNCTION: Functional neuronal receptor which couples to  
 CC intracellular signaling pathway through the GTP-binding protein  
 CC G(O) (By similarity).  
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein.  
 CC -!- SIMILARITY: Belongs to the APP family.  
 CC -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.  
 CC -----  
 CC This SWISS-PROT entry is copyright. It is produced through a collaboration  
 CC between the Swiss Institute of Bioinformatics and the EMBL outstation -  
 CC the European Bioinformatics Institute. There are no restrictions on its  
 CC use by non-profit institutions as long as its content is in no way  
 CC modified and this statement is not removed. Usage by and for commercial  
 CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>  
 CC or send an email to [license@isb-sib.ch](mailto:license@isb-sib.ch)).  
 CC -----  
 DR EMBL; AF090120; AAD13392.1; -.  
 DR HSSP; P05067; 1HZ3.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR InterPro; IPR002223; Kunitz\_BPTI.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR Pfam; PF00014; Kunitz\_BPTI; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR PRINTS; PR00759; BASICPTASE.  
 DR ProDom; PD000222; Kunitz\_BPTI; 1.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR SMART; SM00131; KU; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; FALSE\_NEG.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 DR PROSITE; PS00280; BPTI\_KUNITZ\_1; 1.  
 DR PROSITE; PS00279; BPTI\_KUNITZ\_2; 1.  
 KW Glycoprotein; Amyloid; Neurone; Transmembrane; Signal;  
 KW Serine protease inhibitor.  
 FT SIGNAL 1 18 POTENTIAL.  
 FT CHAIN 19 737 ALZHEIMER'S DISEASE AMYLOID A4  
 FT PROTEIN HOMOLOG.  
 FT CHAIN 639 681 BETA-AMYLOID PROTEIN (POTENTIAL).  
 FT DOMAIN 19 668 EXTRACELLULAR (POTENTIAL).  
 FT TRANSMEM 669 689 POTENTIAL.  
 FT DOMAIN 690 737 CYTOPLASMIC (POTENTIAL).  
 FT DOMAIN 286 344 BPTI/KUNITZ INHIBITOR.  
 FT SITE 726 729 CLATHRIN-BINDING (BY SIMILARITY).  
 FT ACT\_SITE 300 301 REACTIVE BOND.

FT DISULFID 290 340 BY SIMILARITY.  
 FT DISULFID 299 323 BY SIMILARITY.  
 FT DISULFID 315 336 BY SIMILARITY.  
 FT CARBOHYD 522 522 N-LINKED (GLCNAC. . .) (POTENTIAL).  
 SQ SEQUENCE 737 AA; 82856 MW; 6FAD01E2E3B2B7E2 CRC64;

Query Match 67.1%; Score 2448.5; DB 1; Length 737;  
 Best Local Similarity 64.0%; Pred. No. 6.9e-113;  
 Matches 482; Conservative 84; Mismatches 100; Indels 87; Gaps 12;

Qy 7 LLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGKTCTCIDTK 66  
 :||| | :|:|:| | ||| |||:||||:||||:||||:||||:||||:||||:|:|:|  
 Db 8 VLLLVATLTRSSEIPADDTVGLLTPQVAMFCGKLNMHINVQNGKWESDPSGTKSCLNTK 67

Qy 67 EGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVGEFVSDA 126  
 |||||:||||:||||:| | |:|||||  
 Db 68 EGILQYCQEVYPELQITNVVEANQPVSIQNWCKKGRKQCRSHTHIVVPYRCLVGEFVSDA 127

Qy 127 LLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEFVC 186  
 |||||: ||:|||||:| ::| |||||:||||:|  
 Db 128 LLVPDKCKFLHQERMNQCESHLHWHTVAKESCGDRSMNLHDYGMLLPCGIDRFRGVKFVC 187

Qy 187 CPLAEESDNVDSADAEEDSDVWGGADTDYADGS---EDKVVEVAEEEEVAEEEEEEAD 243  
 || || ||:: | ::||| | ::: | : || : | :| |  
 Db 188 CP-AETEQETDSSEVEGEESDVWGGADPEYSENSPPTPSRATYVAGD---AFERDENG 243

Qy 244 DDEDDDEDGDEVEEEAEEPYEEATERTTSIA--TTTTTTTSESVEEVVR----- 288  
 |||:| | ::| | :|: ||| ::| |||||  
 Db 244 GDEDEEDDEDVDPTDE---QESDERTANVAMTTTTTTTTTSESVEEVVRVAVCWAQAESGPCR 300

Qy 289 -----VPTTAASTPDAVDKYLE 305  
 :|| | | |||:| |  
 Db 301 AMLERWYFNPKKRRRCVPFLFGGCGGNRNNFESEYCLAVCSSSLPTVAPSPDAVDQYFE 360

Qy 306 TPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHFQEKVE 365  
 |||:|||| |:||| |||||:|||||  
 Db 361 APGDDNEHADFRKAKESLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHFQEKVE 420

Qy 366 SLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKYVRA 425  
 :||||| |||||:| ||| |||: ||| ||| | | ::|||  
 Db 421 ALEQEAAAGERQQLVETHMARVEALLNSRRRLTLENYLGALQANPPRARQVLSLLKKYVRA 480

Qy 426 EQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLYNVPAVAEEIQD 485  
 |||||:|||| ||||| | |:|||| | ||||:| ||| |:| |||:  
 Db 481 EQKDRQHTLKHFEHVRMVDPKKAAQIRPQVLTHLRVIDERMNQSLALLYKVPVASEIQN 540

Qy 486 EVDELLQKEQNYSDVLANMIS---EPRI SYGN DALMP SLTETKT TVELLPVNGEFSLDD 542  
 :: : | : : : : : ||||| : : : | :| | :|  
 Db 541 QIYPAAGSD---CKDPVEHCVC PQVDGLVSYGN DALMPDQAYSSAPMD-MGVDGLGSID- 595

Qy 543 LQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEFRH 602  
 || |||| ||||| ||| ||| ::::| ||: ||: : : |  
 Db 596 ----QSFN----QANTENHVEPVDARPIPDRLPTRP---VSSLKLEEMPEVRTETDKRQ 644

Qy 603 DSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGVVE 662  
 :|||:|||||:|||||:|||||:|||||:|||||:|||||:|  
 Db 645 SAGYEVYHQKL VFFADDVGSNKGAIIGLMVGGVVIATVIVITLVMLRKKQYTSIHGGVIE 704

Qy 663 VDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695  
 |||||:|||||  
 Db 705 VDAAVTPEERHLARMQQNGYENPTYKFFEQMQN 737

RESULT 10

APP2\_MOUSE

ID APP2\_MOUSE STANDARD; PRT; 695 AA.  
 AC Q06335;  
 DT 01-JUN-1994 (Rel. 29, Created)  
 DT 01-FEB-1996 (Rel. 33, Last sequence update)  
 DT 15-MAR-2004 (Rel. 43, Last annotation update)  
 DE Amyloid-like protein 2 precursor (CDEI-box binding protein) (CDEBP).  
 GN APLP2.  
 OS Mus musculus (Mouse).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.  
 OX NCBI\_TaxID=10090;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RC TISSUE=Fetal brain;  
 RA von der Kammer H.;  
 RL Submitted (JUL-1994) to the EMBL/GenBank/DDBJ databases.  
 RN [2]  
 RP SEQUENCE OF 1-246 FROM N.A.  
 RX MEDLINE=94032480; PubMed=8218408;  
 RA Hanes J., von der Kammer H., Kristjansson G.I., Scheit K.H.;  
 RT "The complete cDNA coding sequence for the mouse CDEI binding  
 RT protein.";  
 RL Biochim. Biophys. Acta 1216:154-156(1993).  
 RN [3]  
 RP SEQUENCE OF 185-695 FROM N.A.  
 RC STRAIN=BALB/c; TISSUE=Heart;  
 RX MEDLINE=93129193; PubMed=1482349;  
 RA Vidal F., Blangy A., Rassoulzadegan M., Cuzin F.;  
 RT "A murine sequence-specific DNA binding protein shows extensive local  
 RT similarities to the amyloid precursor protein.";  
 RL Biochem. Biophys. Res. Commun. 189:1336-1341(1992).  
 RN [4]  
 RP SEQUENCE OF 1-35 FROM N.A.  
 RC STRAIN=129/Sv;  
 RX MEDLINE=96029629; PubMed=7592716;  
 RA von Koch C.S., Lahiri D.K., Mammen A.L., Copeland N.G.,  
 RA Gilbert D.J., Jenkins N.A., Sisodia S.S.;  
 RT "The mouse APLP2 gene. Chromosomal localization and promoter  
 RT characterization.";  
 RL J. Biol. Chem. 270:25475-25480(1995).  
 CC -!- FUNCTION: Binds to the DNA 5'-GTCACATG-3' (CDEI box) which plays  
 CC an important role in the early development of embryos.  
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein and nuclear  
 CC (Potential).  
 CC -!- SIMILARITY: Belongs to the APP family.  
 CC -----  
 CC This SWISS-PROT entry is copyright. It is produced through a collaboration  
 CC between the Swiss Institute of Bioinformatics and the EMBL outstation -  
 CC the European Bioinformatics Institute. There are no restrictions on its

CC use by non-profit institutions as long as its content is in no way  
CC modified and this statement is not removed. Usage by and for commercial  
CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>  
CC or send an email to [license@isb-sib.ch](mailto:license@isb-sib.ch)).  
CC -----

DR EMBL; Z22592; CAA80306.1; -.  
DR EMBL; M97216; AAA20039.1; -.  
DR EMBL; U34291; AAC52318.1; -.  
DR PIR; JC1404; JC1404.  
DR PIR; S38344; S38344.  
DR HSSP; P05067; 1MWP.  
DR MGD; MGI:88047; Aplp2.  
DR InterPro; IPR008155; A4\_APP.  
DR InterPro; IPR008154; A4\_extra.  
DR Pfam; PF02177; A4\_EXTRA; 1.  
DR PRINTS; PR00203; AMYLOIDA4.  
DR SMART; SM00006; A4\_EXTRA; 1.  
DR PROSITE; PS00319; A4\_EXTRA; 1.  
DR PROSITE; PS00320; A4\_INTRA; 1.  
KW Transmembrane; DNA-binding; Signal; Nuclear protein.  
FT SIGNAL 1 29 POTENTIAL.  
FT CHAIN 30 695 AMYLOID-LIKE PROTEIN 2.  
FT DOMAIN 30 624 EXTRACELLULAR (POTENTIAL).  
FT TRANSMEM 625 648 POTENTIAL.  
FT DOMAIN 649 695 CYTOPLASMIC (POTENTIAL).  
FT DOMAIN 218 294 ASP/GLU-RICH (HIGHLY ACIDIC).  
FT DOMAIN 218 231 POLY-GLU.  
FT DOMAIN 256 266 POLY-GLU.  
FT CARBOHYD 485 485 N-LINKED (GLCNAC. . .) (POTENTIAL).  
FT CONFLICT 185 189 GMLLP -> MACCC (IN REF. 3).  
SQ SEQUENCE 695 AA; 78944 MW; BBF4B95AAB2A0311 CRC64;

Query Match 47.5%; Score 1735; DB 1; Length 695;  
Best Local Similarity 49.3%; Pred. No. 5.2e-78;  
Matches 360; Conservative 118; Mismatches 162; Indels 90; Gaps 19;

Qy 5 LALLLLAAWTARALEV-----PTDGNAG---LLAEPQIAMFCGRLNMHMNVQNGKWDSDP 56  
| :||| || | : ||| :||||| ||:||||:| | ||: ||  
Db 15 LLVLLLLGLTAPAAALAGYIEALAANAGTGFVAEAPQIAMLCGKLNMHVNIQTGKWEPPD 74  
  
Qy 57 SGTKTCTIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYR 116  
:||||:| ||| :|||||:|||||||:||||| | :||:| :|||: | |||:  
Db 75 TGTKSCLGTKEEVLQYCQEIYPELQITNVMEANQPVNIDSWCRRDKRQCKS--HIVIPFK 132  
  
Qy 117 CLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLP CGI 176  
||||||| |||| | :| ||||:||| | |||: || | : | : |||||:  
Db 133 CLVGEFVSDVLLVPDNCQFFHQERMEVCEKHQRWHTLVKEACLTEGLTLYSYGMLLP CGV 192  
  
Qy 177 DKFRGVEFVCCPLAE--ESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAE---E 231  
|:| | |:|||| : :||: | : ||:| | | || : : | |  
Db 193 DQFHGTEYVCCPQTKTVDSSTMSKEEEEEEE-----DEEDEEEDYDLKSEFPTE 243  
  
Qy 232 EEVAEVEEEEAD-DEDEDGDEVEEEAE-----EPYEEATERTTSIATTTTTTTES 282  
: : | || :||:|:|:| | : : : | | | | : : | : :  
Db 244 ADLEDFTAAADEEEEEEEGEEVVEDRDYYYDPFKGDDYNE--ENPTEPSSEGTISDKE 301  
  
Qy 283 VEEVVRVPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAE 342



RC TISSUE=Ovary;  
 RX MEDLINE=95217334; PubMed=7702756;  
 RA von der Kammer H., Hanes J., Klaudiny J., Scheit K.H.;  
 RT "A human amyloid precursor-like protein is highly homologous to a  
 RT mouse sequence-specific DNA-binding protein.";  
 RL DNA Cell Biol. 13:1137-1143(1994).  
 RN [3]  
 RP SEQUENCE FROM N.A.  
 RC TISSUE=Brain;  
 RX MEDLINE=94035131; PubMed=8220435;  
 RA Wasco W., Gurubhagavatula S., Paradis M., Romano D.M., Sisodia S.S.,  
 RA Hyman B.T., Neve R.L., Tanzi R.E.;  
 RT "Isolation and characterization of APLP2 encoding a homologue of the  
 RT Alzheimer's associated amyloid beta protein precursor.";  
 RL Nat. Genet. 5:95-99(1993).  
 RN [4]  
 RP SEQUENCE FROM N.A. (ISOFORM 3).  
 RC TISSUE=Lung;  
 RX MEDLINE=22388257; PubMed=12477932;  
 RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,  
 RA Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,  
 RA Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,  
 RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,  
 RA Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,  
 RA Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,  
 RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,  
 RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,  
 RA Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,  
 RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,  
 RA Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,  
 RA Fahey J., Helton E., Kettelman M., Madan A., Rodrigues S., Sanchez A.,  
 RA Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,  
 RA Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,  
 RA Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,  
 RA Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,  
 RA Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;  
 RT "Generation and initial analysis of more than 15,000 full-length  
 RT human and mouse cDNA sequences.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).  
 CC -!- FUNCTION: May play a role in the regulation of hemostasis. The  
 CC soluble form may have inhibitory properties towards coagulation  
 CC factors. May interact with cellular G-protein signaling pathways.  
 CC May bind to the DNA 5'-GTCACATG-3'(CDEI box).  
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein and nuclear  
 CC (Potential).  
 CC -!- ALTERNATIVE PRODUCTS:  
 CC Event=Alternative splicing; Named isoforms=3;  
 CC Comment=Additional isoforms seem to exist;  
 CC Name=1;  
 CC IsoId=Q06481-1; Sequence=Displayed;  
 CC Name=2;  
 CC IsoId=Q06481-2; Sequence=VSP\_000018;  
 CC Name=3;  
 CC IsoId=Q06481-3; Sequence=VSP\_000019;  
 CC -!- TISSUE SPECIFICITY: In placenta, brain, heart, lung, liver, kidney  
 CC and endothelial tissues.  
 CC -!- SIMILARITY: Belongs to the APP family.

```

CC  -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.
CC  -----
CC  This SWISS-PROT entry is copyright. It is produced through a collaboration
CC  between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC  the European Bioinformatics Institute. There are no restrictions on its
CC  use by non-profit institutions as long as its content is in no way
CC  modified and this statement is not removed. Usage by and for commercial
CC  entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC  or send an email to license@isb-sib.ch).
CC  -----
DR  EMBL; S60099; AAC60589.1; -.
DR  EMBL; L09209; AAA35526.1; -.
DR  EMBL; Z22572; CAA80295.1; -.
DR  EMBL; L27631; AAC41701.1; -.
DR  EMBL; BC000373; AAH00373.1; -.
DR  PIR; A49321; A49321.
DR  HSSP; P05067; 1MWP.
DR  Genew; HGNC:598; APLP2.
DR  MIM; 104776; -.
DR  GO; GO:0016021; C:integral to membrane; NAS.
DR  GO; GO:0005634; C:nucleus; IDA.
DR  GO; GO:0003677; F:DNA binding; NAS.
DR  GO; GO:0007186; P:G-protein coupled receptor protein signalin. . .; NAS.
DR  InterPro; IPR008155; A4_APP.
DR  InterPro; IPR008154; A4_extra.
DR  InterPro; IPR002223; Kunitz_BPTI.
DR  Pfam; PF02177; A4_EXTRA; 1.
DR  Pfam; PF00014; Kunitz_BPTI; 1.
DR  PRINTS; PR00203; AMYLOIDA4.
DR  PRINTS; PR00759; BASICPTASE.
DR  ProDom; PD000222; Kunitz_BPTI; 1.
DR  SMART; SM00006; A4_EXTRA; 1.
DR  SMART; SM00131; KU; 1.
DR  PROSITE; PS00319; A4_EXTRA; 1.
DR  PROSITE; PS00320; A4_INTRA; 1.
DR  PROSITE; PS00280; BPTI_KUNITZ_1; 1.
DR  PROSITE; PS00279; BPTI_KUNITZ_2; 1.
KW  Transmembrane; Signal; Alternative splicing; DNA-binding;
KW  Nuclear protein; Serine protease inhibitor.
FT  SIGNAL      1      29      POTENTIAL.
FT  CHAIN       30     763     AMYLOID-LIKE PROTEIN 2.
FT  DOMAIN      30     692     EXTRACELLULAR (POTENTIAL).
FT  TRANSMEM    693     716     POTENTIAL.
FT  DOMAIN      717     763     CYTOPLASMIC (POTENTIAL).
FT  DOMAIN      215     280     ASP/GLU-RICH (HIGHLY ACIDIC).
FT  DOMAIN      306     364     BPTI/KUNITZ INHIBITOR.
FT  DOMAIN      215     231     POLY-GLU.
FT  ACT_SITE    320     321     REACTIVE BOND (BY SIMILARITY).
FT  DISULFID     310     360     BY SIMILARITY.
FT  DISULFID     319     343     BY SIMILARITY.
FT  DISULFID     335     356     BY SIMILARITY.
FT  VARSPLIC     308     363     Missing (in isoform 2).
FT                                     /FTid=VSP_000018.
FT  VARSPLIC     613     624     Missing (in isoform 3).
FT                                     /FTid=VSP_000019.
FT  CONFLICT     543     543     S -> I (IN REF. 1).
SQ  SEQUENCE    763 AA;  86955 MW;  CA3A7D6DDB8A28D0 CRC64;

```

Query Match 47.3%; Score 1728; DB 1; Length 763;  
Best Local Similarity 47.1%; Pred. No. 1.3e-77;  
Matches 372; Conservative 112; Mismatches 165; Indels 140; Gaps 20;

```
Qy      5 LALLLLAAWTARALEV-----PTDGNAG---LLAEPQIAMFCGRLNMHMNVQNGKWSDP 56
      | | | | | | | | : | | | : | | | | | | | | : | | | | | | | |
Db     15 LLLLLLVGLTAPALALAGYIEALAANAGTGFAVAEPQIAMFCGKLNMHVNIQTGWEPDP 74

Qy     57 SGTKTCTIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYR 116
      : | | : | | : | | | | : | | | | | | | | : | | : | | : | |
Db     75 TGTKSCFETKKEEVLQYCQEMYPELQITNVMEANQRVSIDNWCRRDKKQCKS--RFVTPFK 132

Qy    117 CLVGFEFVSDALLVPDKCKFLHQERMDVCEHLHWHTVAKETCSEKSTNLHDYGMLLPCGI 176
      | | | | | | | | | | : | | : | | : | | | | | | | : | | : | | | | :
Db    133 CLVGFEFVSDVLLVPEKQCFHFKERMEVCENHQHWHTVVKEACLTQGMTLYSYGMLLPCGV 192

Qy    177 DKFRGVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAE 236
      | : | | | : | | | : | | : | | : | | : | | : | | : | |
Db    193 DQFHGTEYVCCPQTKIIGSVSKEEEEEDEE-----EEEEEEEEEDYDVYKSEFPTEAD 245

Qy    237 VEE--EEA--DDDEDDDEDGDEVEEEAEPEY-----EEATERTTSIATTTTTTTES 282
      : | : | | : | | | : | | | : | | : | | : | | : | | : | |
Db    246 LEDFTEAAVDEDDDEDEEEGEEVVEDRDYYYDTFKGDDYNEENPTEPGSDGTMSDKEITHD 305

Qy    283 VEEV-----VRVP 290
      | : | | | | | | | | | | | | | | | | | | | | | | | | | |
Db    306 VKAVCSQEAMTGPCRAVMPRWYFDLSKGKCVRFIYGGCGGNRNNFESDYCMAVCKAMIP 365

Qy    291 TTAASTPDAVDKYLETPGDENEAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPK 350
      | | | | | | | | | | : | | | | | | | | : | | | | : | | | | | | | |
Db    366 PTPLPTND-VDVYFETSADDNEHARFQKAKEQLEIRHRNRMDRVKKEWEEAELQAKNLPK 424

Qy    351 ADKKAVIDQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPP 410
      | : : : | | | | | : | : | : | : | : | : | : | : | : | : | : | |
Db    425 AERQTLIQHFQAMVKALEKEAASEKQQLVETHLARVEAMLNDRRRMALENYLAALQSDPP 484

Qy    411 RPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQL 470
      | | : | : | | | | | | | : | : | : | | | | : | | | | | | | | | |
Db    485 RPHRILQALRRYVRAENKDRHTIRHYQHVLAVDPEKAAQMKSQVMTHLHVIEERRNQL 544

Qy    471 SLLYNVPAVAEEIQDEVDLLOKEQNYSDVLNMISEPRISYGNALMPSLTETKTVE 530
      | | | | | | | | : | : | : | : | : | : | : | : | : | : | : | : |
Db    545 SLLYKVPYVAQEIQEEIDELLQEQR-----ADM-----DQFTASISETPVDVR 587

Qy    531 LLPVNGEFSLDDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTN----- 585
      | : | | : : | : | | | | | | | | : | : | : | : | : | : | : |
Db    588 ---VSSEES-EEIPPFHFP--HFPFALPENE----DTQPELYHPM--KKGSGVGEQDGG 635

Qy    586 IKTEE---ISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGS-----NKG 625
      | | | | | : | : | | : | : : : | | | | | : | : | : | : |
Db    636 IGAEKVINSKNKVDENMVIDETLDV--KEMIFNAERVGGLEEEERESVGPLREDFSLSS 693

Qy    626 AIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENP 685
      | : | | : | | | | | : | | : | : | : | : | : | : | : | : | : |
Db    694 ALIGLLVIAVAIATVIVISLVMLRKRQYGTISHGIVEVDPMLTPEERHLNKMQNHYENP 753
```



Qy 686 TYKFFEQMQ 694  
|||: ||||  
Db 754 TYKYLEQMQ 762

RESULT 12

APP2\_RAT

ID APP2\_RAT STANDARD; PRT; 765 AA.  
AC P15943;  
DT 01-APR-1990 (Rel. 14, Created)  
DT 01-OCT-1996 (Rel. 34, Last sequence update)  
DT 28-FEB-2003 (Rel. 41, Last annotation update)  
DE Amyloid-like protein 2 precursor (Sperm membrane protein YWK-II).  
GN APLP2.  
OS Rattus norvegicus (Rat).  
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.  
OX NCBI\_TaxID=10116;  
RN [1]  
RP SEQUENCE OF 1-627 FROM N.A.  
RC STRAIN=Wistar; TISSUE=Brain, and Heart;  
RX MEDLINE=94368849; PubMed=8086458;  
RA Sandbrink R., Masters C.L., Beyreuther K.;  
RT "Complete nucleotide and deduced amino acid sequence of rat amyloid  
RT protein precursor-like protein 2 (APLP2/APPH): two amino acids length  
RT difference to human and murine homologues.";  
RL Biochim. Biophys. Acta 1219:167-170(1994).  
RN [2]  
RP SEQUENCE OF 575-765 FROM N.A.  
RC TISSUE=Testis;  
RX MEDLINE=90207205; PubMed=1690887;  
RA Yan Y.C., Bai Y., Wang L.F., Miao S.Y., Koide S.S.;  
RT "Characterization of cDNA encoding a human sperm membrane protein  
RT related to A4 amyloid protein.";  
RL Proc. Natl. Acad. Sci. U.S.A. 87:2405-2408(1990).  
CC -!- SUBCELLULAR LOCATION: Type I membrane protein.  
CC -!- ALTERNATIVE PRODUCTS:  
CC Event=Alternative splicing; Named isoforms=4;  
CC Name=A;  
CC IsoId=P15943-1; Sequence=Displayed;  
CC Name=B;  
CC IsoId=P15943-2; Sequence=VSP\_000021;  
CC Name=C;  
CC IsoId=P15943-3; Sequence=VSP\_000020;  
CC Name=D;  
CC IsoId=P15943-4; Sequence=VSP\_000020, VSP\_000021;  
CC -!- SIMILARITY: Belongs to the APP family.  
CC -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.  
CC -----  
CC This SWISS-PROT entry is copyright. It is produced through a collaboration  
CC between the Swiss Institute of Bioinformatics and the EMBL outstation -  
CC the European Bioinformatics Institute. There are no restrictions on its  
CC use by non-profit institutions as long as its content is in no way  
CC modified and this statement is not removed. Usage by and for commercial  
CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>  
CC or send an email to [license@isb-sib.ch](mailto:license@isb-sib.ch)).  
CC -----

DR EMBL; X77934; CAA54906.1; -.  
 DR EMBL; M31322; AAA42352.1; -.  
 DR PIR; A35981; A35981.  
 DR PIR; S42880; S42880.  
 DR HSSP; P05067; 1MWP.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR002223; Kunitz\_BPTI.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF00014; Kunitz\_BPTI; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR PRINTS; PR00759; BASICPTASE.  
 DR ProDom; PD000222; Kunitz\_BPTI; 1.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR SMART; SM00131; KU; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 DR PROSITE; PS00280; BPTI\_KUNITZ\_1; 1.  
 DR PROSITE; PS50279; BPTI\_KUNITZ\_2; 1.  
 KW Transmembrane; Alternative splicing; Serine protease inhibitor;  
 KW Signal; Glycoprotein.  
 FT SIGNAL 1 29 POTENTIAL.  
 FT CHAIN 30 765 AMYLOID-LIKE PROTEIN 2.  
 FT DOMAIN 30 695 EXTRACELLULAR (POTENTIAL).  
 FT TRANSMEM 696 718 POTENTIAL.  
 FT DOMAIN 719 765 CYTOPLASMIC (POTENTIAL).  
 FT DOMAIN 218 282 ASP/GLU-RICH (HIGHLY ACIDIC).  
 FT DOMAIN 308 366 BPTI/KUNITZ INHIBITOR.  
 FT ACT\_SITE 322 323 REACTIVE BOND (BY SIMILARITY).  
 FT DISULFID 312 362 BY SIMILARITY.  
 FT DISULFID 321 345 BY SIMILARITY.  
 FT DISULFID 337 358 BY SIMILARITY.  
 FT DOMAIN 218 229 POLY-GLU.  
 FT CARBOHYD 628 628 O-LINKED (GLYCOSAMINOGLYCAN) (POTENTIAL).  
 FT VARSPLIC 311 365 Missing (in isoform C and isoform D).  
 FT /FTId=VSP\_000020.  
 FT VARSPLIC 616 627 Missing (in isoform B and isoform D).  
 FT /FTId=VSP\_000021.  
 FT CONFLICT 575 577 DQF -> EFV (IN REF. 2).  
 SQ SEQUENCE 765 AA; 86882 MW; CF51FCCCE305A0CF CRC64;

Query Match 47.0%; Score 1716; DB 1; Length 765;  
 Best Local Similarity 46.2%; Pred. No. 4.9e-77;  
 Matches 364; Conservative 122; Mismatches 166; Indels 136; Gaps 20;

Qy 5 LALLLLAAWTARALEV-----PTDGNAG---LLAEPQIAMFCGRLNMHMNVQNGKWDS DP 56  
 | :||| || | : ||| :|||||||:||||:| | ||: ||  
 Db 15 LLVLLLLGLTAPAAALAGYIEALAAANAGTGFAVAEPQIAMFCGKLNMHVNIQTGWEP DP 74  
 Qy 57 SGTKTCTIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYR 116  
 :|||:| :|| :|||||:|||||||:||||| | :||:| :|||: | |||:  
 Db 75 TGTKSCLGTKEEVLQYCQEIYPELQITNVMEANQPVNIDSWCRRDKKQCRS--HIVIPFK 132  
 Qy 117 CLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGI 176  
 ||||| |||: | :| ||||: || | |||| || | : | : |||||:  
 Db 133 CLVGEFVSDVLLVPENCQFFHQERMEVCEKHQRWHTVVKEACLTEGMTLYSYGMLLPCGV 192



OX NCBI\_TaxID=9606;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RX MEDLINE=98088960; PubMed=9428684;  
 RA Paliga K., Peraus G., Kreger S., Duwrrwang U., Hesse L., Multhaup G.,  
 RA Masters C.L., Beyreuther K., Weidemann A.;  
 RT "Human amyloid precursor-like protein 1 -- cDNA cloning, ectopic  
 RT expression in COS-7 cells and identification of soluble forms in the  
 RT cerebrospinal fluid.";  
 RL Eur. J. Biochem. 250:354-363(1997).  
 RN [2]  
 RP SEQUENCE FROM N.A.  
 RX MEDLINE=98180887; PubMed=9521588;  
 RA Lenkkeri U., Kestila M., Lamerdin J., McCready P., Adamson A.,  
 RA Olsen A., Tryggvason K.;  
 RT "Structure of the human amyloid-precursor-like protein gene APLP1 at  
 RT 19q13.1.";  
 RL Hum. Genet. 102:192-196(1998).  
 RN [3]  
 RP SEQUENCE FROM N.A.  
 RC TISSUE=Ovary;  
 RX MEDLINE=22388257; PubMed=12477932;  
 RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,  
 RA Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,  
 RA Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,  
 RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,  
 RA Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,  
 RA Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,  
 RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,  
 RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,  
 RA Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,  
 RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,  
 RA Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,  
 RA Fahey J., Helton E., Kettelman M., Madan A., Rodrigues S., Sanchez A.,  
 RA Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,  
 RA Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,  
 RA Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,  
 RA Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,  
 RA Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;  
 RT "Generation and initial analysis of more than 15,000 full-length  
 RT human and mouse cDNA sequences.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).  
 RN [4]  
 RP POSSIBLE FUNCTION, AND TISSUE SPECIFICITY.  
 RX MEDLINE=96115107; PubMed=7494461;  
 RA Kim T.-W., Wu K., Xu J.-L., McAuliffe G., Tanzi R.E., Wasco W.,  
 RA Black I.B.;  
 RT "Selective localization of amyloid precursor-like protein 1 in the  
 RT cerebral cortex postsynaptic density.";  
 RL Brain Res. Mol. Brain Res. 32:36-44(1995).  
 RN [5]  
 RP HEPARIN AND ZINC BINDING.  
 RX MEDLINE=95014513; PubMed=7929392;  
 RA Bush A.I., Pettingell W.H. Jr., de Paradis M., Tanzi R.E., Wasco W.;  
 RT "The amyloid beta-protein precursor and its mammalian homologues.  
 RT Evidence for a zinc-modulated heparin-binding superfamily.";  
 RL J. Biol. Chem. 269:26618-26621(1994).

RN [6]  
 RP INTERACTION WITH APBA2.  
 RX MEDLINE=99107877; PubMed=9890987;  
 RA Tomita S., Ozaki T., Taru H., Oguchi S., Takeda S., Yagi Y.,  
 RA Sakiyama S., Kirino Y., Suzuki T.;  
 RT "Interaction of a neuron-specific protein containing PDZ domains with  
 RT Alzheimer's amyloid precursor protein.";  
 RL J. Biol. Chem. 274:2243-2254(1999).  
 RN [7]  
 RP EXTRACELLULAR COPPER-BINDING.  
 RX MEDLINE=22130992; PubMed=12135352;  
 RA Simons A., Ruppert T., Schmidt C., Schlicksupp A., Pipkorn R.,  
 RA Reed J., Masters C.L., White A.R., Cappai R., Beyreuther K.,  
 RA Bayer T.A., Multhaup G.;  
 RT "Evidence for a copper-binding superfamily of the amyloid precursor  
 RT protein.";  
 RL Biochemistry 41:9310-9320(2000).  
 CC -!- FUNCTION: May play a role in postsynaptic function. The C-terminal  
 CC gamma-secretase processed fragment, ALID1, activates transcription  
 CC activation through APBB1 (Fe65) binding (By similarity). Couples  
 CC to JIP signal transduction through C-terminal binding. May  
 CC interact with cellular G-protein signaling pathways. Can regulate  
 CC neurite outgrowth through binding to components of the  
 CC extracellular matrix such as heparin and collagen I.  
 CC -!- FUNCTION: The gamma-CTF peptide, C30, is a potent enhancer of  
 CC neuronal apoptosis (By similarity).  
 CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several  
 CC cytoplasmic proteins, including APBB and APBA family members,  
 CC MAPK8IP1 and Dab1 (By similarity). Binding to Dab1 inhibits its  
 CC serine phosphorylation (By similarity).  
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein. C-terminally  
 CC processed in the Golgi complex.  
 CC -!- TISSUE SPECIFICITY: Expressed in the cerebral cortex where it is  
 CC localized to the postsynaptic density (PSD).  
 CC -!- DOMAIN: The NPXY sequence motif found in many tyrosine-  
 CC phosphorylated proteins is required for the specific binding of  
 CC the PID domain. However additional amino acids either N- or C-  
 CC terminal to the NPXY motif are often required for complete  
 CC interaction. The NPXY site is also involved in clathrin-mediated  
 CC endocytosis.  
 CC -!- PTM: Proteolytically cleaved by caspases during neuronal  
 CC apoptosis. Cleaved, in vitro, at Asp-620 by caspase-3 (By  
 CC similarity).  
 CC -!- PTM: N- and O-glycosylated.  
 CC -!- MISCELLANEOUS: Binds zinc and copper in the extracellular domain.  
 CC Zinc-binding increases heparin binding. No Cu(II) reducing  
 CC activity with copper-binding.  
 CC -!- SIMILARITY: Belongs to the APP family.  
 CC -----  
 CC This SWISS-PROT entry is copyright. It is produced through a collaboration  
 CC between the Swiss Institute of Bioinformatics and the EMBL outstation -  
 CC the European Bioinformatics Institute. There are no restrictions on its  
 CC use by non-profit institutions as long as its content is in no way  
 CC modified and this statement is not removed. Usage by and for commercial  
 CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>  
 CC or send an email to [license@isb-sib.ch](mailto:license@isb-sib.ch)).  
 CC -----





RC TISSUE=Brain;  
 RX MEDLINE=93066322; PubMed=1279693;  
 RA Wasco W., Bupp K., Magendantz M., Gusella J.F., Tanzi R.E.,  
 RA Solomon F.;  
 RT "Identification of a mouse brain cDNA that encodes a protein related  
 RT to the Alzheimer disease-associated amyloid beta protein precursor.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 89:10758-10762(1992).  
 RN [2]  
 RP SEQUENCE FROM N.A.  
 RC TISSUE=Retina;  
 RX MEDLINE=22388257; PubMed=12477932;  
 RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,  
 RA Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,  
 RA Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,  
 RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,  
 RA Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,  
 RA Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,  
 RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,  
 RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,  
 RA Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,  
 RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,  
 RA Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,  
 RA Fahey J., Helton E., Kettman M., Madan A., Rodrigues S., Sanchez A.,  
 RA Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,  
 RA Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,  
 RA Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,  
 RA Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,  
 RA Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;  
 RT "Generation and initial analysis of more than 15,000 full-length  
 RT human and mouse cDNA sequences.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).  
 RN [3]  
 RP COLLAGEN-BINDING.  
 RX MEDLINE=96139497; PubMed=8576160;  
 RA Beher D., Hesse L., Masters C.L., Multhaup G.;  
 RT "Regulation of amyloid protein precursor (APP) binding to collagen and  
 RT mapping of the binding sites on APP and collagen type I.";  
 RL J. Biol. Chem. 271:1613-1620(1996).  
 RN [4]  
 RP INTERACTION WITH DAB1.  
 RX MEDLINE=99389880; PubMed=10460257;  
 RA Homayouni R., Rice D.S., Sheldon M., Curran T.;  
 RT "Disabled-1 binds to the cytoplasmic domain of amyloid precursor-like  
 RT protein 1.";  
 RL J. Neurosci. 19:7507-7515(1999).  
 RN [5]  
 RP INTERACTION WITH MAPK8IP1.  
 RX MEDLINE=21408156; PubMed=11517249;  
 RA Matsuda S., Yasukawa T., Homma Y., Ito Y., Niikura T., Hiraki T.,  
 RA Hirai S., Ohno S., Kita Y., Kawasumi M., Kouyama K., Yamamoto T.,  
 RA Kyriakis J.M., Nishimoto I.;  
 RT "C-jun N-terminal kinase (JNK)-interacting protein-1b/islet-brain-1  
 RT scaffolds Alzheimer's amyloid precursor protein with JNK.";  
 RL J. Neurosci. 21:6597-6607(2001).  
 RN [6]  
 RP GAMMA-SECRETASE PROCESSING, INTERACTION WITH APBB1, AND MUTAGENESIS OF  
 RP TYR-641.



RX MEDLINE=22313598; PubMed=12228233;  
 RA Scheinfeld M.H., Gherzi E., Laky K., Fowlkes B.J., D'Adamio L.;  
 RT "Processing of beta-amyloid precursor-like protein-1 and -2 by gamma-  
 RT secretase regulates transcription.";  
 RL J. Biol. Chem. 277:44195-44201(2002).  
 CC -!- FUNCTION: May play a role in postsynaptic function. The C-terminal  
 CC gamma-secretase processed fragment, ALID1, activates transcription  
 CC activation through APBB1 (Fe65) binding. Couples to JIP signal  
 CC transduction through C-terminal binding. May interact with  
 CC cellular G-protein signaling pathways. Can regulate neurite  
 CC outgrowth through binding to components of the extracellular  
 CC matrix such as heparin and collagen I.  
 CC -!- FUNCTION: The gamma-CTF peptide, C30, is a potent enhancer of  
 CC neuronal apoptosis (By similarity).  
 CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several  
 CC cytoplasmic proteins, including APBB and APBA family members,  
 CC MAPK8IP1 and Dab1 (By similarity). Binding to Dab1 inhibits its  
 CC serine phosphorylation.  
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein. C-terminally  
 CC processed in the Golgi complex.  
 CC -!- DOMAIN: The NPXY sequence motif found in many tyrosine-  
 CC phosphorylated proteins is required for the specific binding of  
 CC the PID domain. However additional amino acids either N- or C-  
 CC terminal to the NPXY motif are often required for complete  
 CC interaction. The NPXY site is also involved in clathrin-mediated  
 CC endocytosis.  
 CC -!- PTM: Proteolytically cleaved by caspases during neuronal  
 CC apoptosis. Cleaved, in vitro, at Asp-623 by caspase-3 (By  
 CC similarity).  
 CC -!- PTM: N- and O-glycosylated.  
 CC -!- MISCELLANEOUS: Binds zinc and copper in the extracellular domain.  
 CC Zinc-binding increases heparin binding. No Cu(II) reducing  
 CC activity with copper-binding.  
 CC -!- SIMILARITY: Belongs to the APP family.  
 CC -----  
 CC This SWISS-PROT entry is copyright. It is produced through a collaboration  
 CC between the Swiss Institute of Bioinformatics and the EMBL outstation -  
 CC the European Bioinformatics Institute. There are no restrictions on its  
 CC use by non-profit institutions as long as its content is in no way  
 CC modified and this statement is not removed. Usage by and for commercial  
 CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>  
 CC or send an email to [license@isb-sib.ch](mailto:license@isb-sib.ch)).  
 CC -----  
 DR EMBL; L04538; AAA37247.1; -.  
 DR EMBL; BC021877; AAH21877.1; -.  
 DR PIR; A46362; A46362.  
 DR HSSP; P05067; 1MWP.  
 DR MGD; MGI:88046; Aplp1.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 KW Apoptosis; Endocytosis; Cell adhesion; Coated pits; Neurone;  
 KW Heparin-binding; Metal-binding; Copper; Zinc; Signal; Transmembrane;

KW	Glycoprotein.			
FT	SIGNAL	1	37	POTENTIAL.
FT	CHAIN	38	653	AMYLOID-LIKE PROTEIN 1.
FT	CHAIN	624	653	C30 (BY SIMILARITY).
FT	DOMAIN	38	583	EXTRACELLULAR (POTENTIAL).
FT	TRANSMEM	584	606	POTENTIAL.
FT	DOMAIN	607	653	CYTOPLASMIC (POTENTIAL).
FT	DOMAIN	157	177	COPPER-BINDING.
FT	DOMAIN	203	210	ZINC-BINDING (BY SIMILARITY).
FT	DOMAIN	313	345	HEPARIN-BINDING (BY SIMILARITY).
FT	DOMAIN	413	444	HEPARIN-BINDING (BY SIMILARITY).
FT	DOMAIN	445	462	COLLAGEN-BINDING (BY SIMILARITY).
FT	DOMAIN	263	271	POLY-GLU.
FT	DOMAIN	535	538	POLY-SER.
FT	DOMAIN	601	606	POLY-LEU.
FT	SITE	166	166	REQUIRED FOR COPPER(II) REDUCTION (BY
FT				SIMILARITY).
FT	SITE	607	618	BASOLATERAL SORTING SIGNAL (BY
FT				SIMILARITY).
FT	SITE	623	624	CLEAVAGE (BY CASPASE-3) (BY SIMILARITY).
FT	SITE	641	644	ENDOCYTOSIS SIGNAL.
FT	SITE	643	646	NPXY MOTIF.
FT	CARBOHYD	464	464	N-LINKED (GLCNAC. . .) (POTENTIAL).
FT	CARBOHYD	554	554	N-LINKED (GLCNAC. . .) (POTENTIAL).
FT	MUTAGEN	641	641	Y->G: REDUCED BINDING OF APBB1.
FT	CONFLICT	17	17	P -> PP (IN REF. 2).
SQ	SEQUENCE	653 AA;	72750 MW;	56516DC3EA40E4B0 CRC64;

Query Match 32.5%; Score 1185; DB 1; Length 653;  
 Best Local Similarity 38.6%; Pred. No. 3.9e-51;  
 Matches 270; Conservative 121; Mismatches 231; Indels 78; Gaps 17;

Qy	1	MLPGLALLLLAAWTARA-LEVPTDGNAGLLAEPQIAMFCGRLLNMHMNVQNGKWDSDPSGT	59
		:    :           :           :       :  ::  : :    :	
Db	22	LLP-LSLLLLRAQLAVGNLAVGSPSAEAPGSAQVAGLCGRLLTLHRDLRTGRWEPDPQRS	80
Qy	60	KTCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHF-VIPYRCL	118
		:  : :  : : : :         :    : :            : :	
Db	81	RRCLLDPQRVLEYCRQMPYELHIARVEQAAQAI PMERWCGGTRSGRCAHPHHEVVPFHCL	140
Qy	119	VGEFVSDALLVDPKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDK	178
		:    :  :          :    :     :           :	
Db	141	PGEFVSEALLVPEGCRFLHQERMDQCESSTRRHQEAQEACSSQGLILHGSGMLLPCGSDR	200
Qy	179	FRGVEFVCCPLAEESDNVDSADAEEDDSVW-WGGADTDYADGSEDKVVEVAEEEEVAEV	237
		:     :     : :       :	
Db	201	FRGVEYVCCP-PPATPNPSGMAAGDPSTRSWPLGGR----AEGGED-----EEEVESF	248
Qy	238	EEEEADDDDEDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASP	297
		:   : :         :   : :	
Db	249	PQPVDYFVEPPQAEIIIIIIIIERAPPPSSHTPVMVSRVTPTPR-----PT-----	294
Qy	298	DAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVI	357
		:      :      : ::     :  :      : :	
Db	295	DGVDVYFGMPGEIGEHEGFLRAKMDLEERRMRQINEVMREWAMADSQSKNLPKADROALN	354
Qy	358	QHFQEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFN	417

```

      :|||  ::||:: : |||:||||  || |:|:|:|  ||| :: |||  ||:  |
Db      355 EHFQSILQTL EEQVSGERQRLVETHATRVIALINDQRRAALEGFLAALQGDPQAERVLM 414
Qy      418 MLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVP 477
      |:|:|:|:|:|:|:|:|:|:|  |||:|  |:|  ||  |||:|  |||||  ||  |
Db      415 ALRRYLRAEQKEQRHTLRHYQHVAAVDPEKAQQMRFQVQTHLQVIEERMNQSLGLLDQNP 474
Qy      478 AVAEEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMP-SLTETKTTVELLPVNG 536
      |:|:|:|:|  ||  :  :  || :|  | :|  |
Db      475 HLAQELRPQIQELL-----LAEHLGPSEL----DASVPGSSSEDK----- 510
Qy      537 EFSLDDLPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKM 596
      |||  |:|:|  |  :|  | :|  |  : :
Db      511 ----GSLQP-----PESKDDPPVTLP---KGSTDQESSSSGREKLTPL EQYEQ 551
Qy      597 DAEFRHDSGYEVHH---QKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVML-KKKQ 652
      |:|  |:|  |:|:|:|:|  :||:|:|:|  |||
Db      552 KVNASAPRGFPFHSSDIQRDELAPSGTGVSREALSGLLIMGAGGSLIVLSLLLLLRKKKP 611
Qy      653 YTSIHG VVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQ 692
      |:|  |||||  |:|  ||:|  :|:|:|:|:|:|  |:|
Db      612 YGTISHGVVEVDPMLTLEEQQRLRELQRHGYENPTYRFLEE 651

```

RESULT 15

A4\_CAEEL

```

ID      A4_CAEEL          STANDARD;          PRT;    686 AA.
AC      Q10651; Q18583; Q95ZX1;
DT      28-FEB-2003 (Rel. 41, Created)
DT      28-FEB-2003 (Rel. 41, Last sequence update)
DT      28-FEB-2003 (Rel. 41, Last annotation update)
DE      Beta-amyloid-like protein precursor.
GN      APL-1 OR C42D8.8.
OS      Caenorhabditis elegans.
OC      Eukaryota; Metazoa; Nematoda; Chromadorea; Rhabditida; Rhabditoidea;
OC      Rhabditidae; Peloderinae; Caenorhabditis.
OX      NCBI_TaxID=6239;
RN      [1]
RP      SEQUENCE OF 6-686 FROM N.A.
RC      STRAIN=Bristol N2;
RX      MEDLINE=94089766; PubMed=8265668;
RA      Daigle I., Li C.;
RT      "apl-1, a Caenorhabditis elegans gene encoding a protein related to
RT      the human beta-amyloid protein precursor.";
RL      Proc. Natl. Acad. Sci. U.S.A. 90:12045-12049(1993).
RN      [2]
RP      SEQUENCE FROM N.A.
RC      STRAIN=Bristol N2;
RA      Hallsworth K.;
RL      Submitted (MAY-1996) to the EMBL/GenBank/DDBJ databases.
RN      [3]
RP      REVISIONS, AND ALTERNATIVE SPLICING.
RA      Waterston R.;
RL      Submitted (JUN-2001) to the EMBL/GenBank/DDBJ databases.
CC      -!- SUBCELLULAR LOCATION: Type I membrane protein (Potential).
CC      -!- ALTERNATIVE PRODUCTS:
CC      Event=Alternative splicing; Named isoforms=2;

```

```

CC      Name=a;
CC      IsoId=Q10651-1; Sequence=Displayed;
CC      Name=b;
CC      IsoId=Q10651-2; Sequence=VSP_000017;
CC      Note=No experimental confirmation available;
CC      -!- SIMILARITY: Belongs to the APP family.
CC      -----
CC      This SWISS-PROT entry is copyright. It is produced through a collaboration
CC      between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC      the European Bioinformatics Institute. There are no restrictions on its
CC      use by non-profit institutions as long as its content is in no way
CC      modified and this statement is not removed. Usage by and for commercial
CC      entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC      or send an email to license@isb-sib.ch).
CC      -----
DR      EMBL; U00240; AAC46470.1; ALT_INIT.
DR      EMBL; U56966; AAA98722.1; -.
DR      EMBL; U56966; AAK68242.1; -.
DR      PIR; T15795; T15795.
DR      HSSP; P05067; 1MWP.
DR      WormPep; C42D8.8a; CE04209.
DR      WormPep; C42D8.8b; CE27845.
DR      InterPro; IPR008155; A4_APP.
DR      InterPro; IPR008154; A4_extra.
DR      Pfam; PF02177; A4_EXTRA; 1.
DR      PRINTS; PR00203; AMYLOIDA4.
DR      SMART; SM00006; A4_EXTRA; 1.
DR      PROSITE; PS00319; A4_EXTRA; 1.
KW      Signal; Transmembrane; Amyloid; Neurogenesis; Glycoprotein;
KW      Alternative splicing.
FT      SIGNAL      1      21      POTENTIAL.
FT      CHAIN      22      686      BETA-AMYLOID-LIKE PROTEIN.
FT      DOMAIN      22      621      EXTRACELLULAR (POTENTIAL).
FT      TRANSMEM      622      642      POTENTIAL.
FT      DOMAIN      643      686      CYTOPLASMIC (POTENTIAL).
FT      DOMAIN      205      228      ASP-RICH.
FT      DOMAIN      676      679      CLATHRIN-BINDING (POTENTIAL).
FT      CARBOHYD      84      84      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT      CARBOHYD      201      201      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT      CARBOHYD      249      249      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT      CARBOHYD      417      417      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT      VARSPLIC      538      539      Missing (in isoform b).
FT      /FTId=VSP_000017.
SQ      SEQUENCE      686 AA; 79434 MW; A0816858FDD48608 CRC64;

```

```

Query Match      22.4%; Score 817.5; DB 1; Length 686;
Best Local Similarity 29.1%; Pred. No. 3.9e-33;
Matches 222; Conservative 110; Mismatches 275; Indels 155; Gaps 22;

```

```

Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
      :: || : : | | | | | | | | : | || | : | : | | : |
Db      6 LMIGLLIPILVA-TVYAEGSPAGSKRHEKFIPMVAFSCGYRNQYM-TEEGSWKTDDERYA 63

Qy      61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
      || | ||:|:|: || : |||:| | : | : | : | | | | | : |
Db      64 TCFSGKLDILKYCRKAYPSMNITNIVEYSHEVSISDWCREEGSPCK-WTHSVRPYHCIDG 122

```

Qy 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTN-----LHDYGMLLPC 174  
 || |:|| || |:| | | : || | : | | : : :| ||  
 Db 123 EFHSEALQVPHDCQFQSHVNSRDQCNDYQHWKDEAGKQCKTKKSKGNKDMIVRSFAVLEPC 182

Qy 175 GIDKFRGVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEV 234  
 :| | ||||| | :| : | : :  
 Db 183 ALDMFTGVEFVCCP-----NDQTNKTDVQKTK----- 209

Qy 235 AEVEEEEADDEDEDGDEVEEEAEFPYEEATERTTSIATTTTTTTTESVEEVVRVPTTAA 294  
 |:|: ||||| | : ||:| ||  
 Db 210 ---EDEDDEDDDAYEDDYSEESDEKDEE----- 236

Qy 295 STPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEA-----ERQAKNLP 349  
 | : | | : ||| |:|: |:| |||:: :|:| | : |:|:| |  
 Db 237 -EPSSQDPYFKIANWTNEHDDFKKAEMRMDEKHKRKKVDKVMKEWGDLETRYNEQKAKD-P 294

Qy 350 KADKKAVIQ---HFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITAL- 405  
 | :| | | |:| | ||:| |::| | |:| |||:::| | :| ||  
 Db 295 KGAEKFKSQMNARFQKTVSSLEEEHKRMRKEIEAVHEERVQAMLNEKKRDATHDYRQALA 354

Qy 406 -QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYE 464  
 | | | |:|:| ||| | :| : | |:| | : | : || |  
 Db 355 THVNKPNKHSVLQSLKAYIRAEKDRMHTLNRYRHLLKADSKEAAAYKPTVIHRLRYIDL 414

Qy 465 RMNQSLSLLYNVP-----AVA--EEIQDEVDELLOKEQNYSDDLANMISEPRISY 513  
 |:| :|:| : | || : : :||| : | | | :| : |  
 Db 415 RINGTLAMLRDFPDLEKYVRPIAVTYWKDYRDEVSPDISVE----DSELTPIIHDEFSK 470

Qy 514 GN--DALMPSLT----ETKTTVELLPVNGEFSLDDLQPWHSFGADSV PANT---ENEVEP 564  
 | |:| : :|| | : : : | | : :| : :|  
 Db 471 NAKLDVKAPTTTAKPVKETDNAKVLPTASDSEEEADEYYEDEDDEQVKKTPDMKKKVKV 530

Qy 565 VDARP-----AADRGLTTRPGSGLTNIKTEE-----ISEVKMDA 598  
 || :| | | | |: :|| | | |:| :|  
 Db 531 VDIKPKEIKVTIEEEKKAPKLVETSVQTDDDDDEDSSSSTSSSEDEDEDKNIKELRVDI 590

Qy 599 E-----FRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLK 649  
 | :|| | :| | | : : | | | :  
 Db 591 EPIIDEPASFYRHD-----KLIQSFEVERSASSVFQPYVLASAMFITAICIIAFAIT 642

Qy 650 KKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFE 691  
 : | :|| | |||||: || ||||| ||:  
 Db 643 NARRRRAMRGFIEVD-VYTPEERHVAGMQVNGYENPTYSFDD 683

Search completed: July 26, 2004, 12:44:37  
 Job time : 13 secs